

Clinical Trial Protocol

Iranian Registry of Clinical Trials

29 Aug 2026

Comparing the effect of Empagliflozin with Pioglitazone on nonalcoholic fatty liver in diabetic type 2 patients treated with metformin

Protocol summary

Study aim

Comparing the Empagliflozin with Pioglitazone effect on nonalcoholic fatty liver in diabetic type 2 patients treated with metformin

Design

An open-label, randomized clinical trial study with parallel groups and phases 3 on 60 patients. Randomization will be done with the block randomization method using Random allocation software.

Settings and conduct

This open-label, randomized clinical trial study will be conducted on 60 patients of type 2 diabetics and at least grade 1 of non-alcoholic fatty liver disease in Urmia Imam Khomeini Hospital.

Participants/Inclusion and exclusion criteria

In this study, 60 patients treated with metformin for at least three months with a minimum dose of 1500 mg daily and with at least grade 1 non-alcoholic fatty liver will be included. The main exclusion criteria included patients receiving drugs that stimulate insulin secretion, or insulin, type 1 diabetes, patients treated with diabetes drugs including sitagliptin and liraglutide, and other liver diseases including autoimmune hepatitis and viral hepatitis.

Intervention groups

In group one, patients will receive 30 mg pioglitazone daily, and in group two, 10 mg empagliflozin daily in addition to the standard treatment (metformin) for 6 months. If Hb A1c is not controlled after three months of intervention, the dose of metformin will be increased from 1500 to 2500 and the dose of empagliflozin will be increased from 10 to 25 mg. Patients who will not take at least 80% of the tablets during the study will be excluded.

Main outcome variables

liver steatosis score; Liver enzymes including Alanine transaminase (ALT); Aspartate transaminase (AST); Alkaline phosphatase (ALKP).

General information

Reason for update

According to the necessity of proper blood sugar control of patients with diabetes (with any grade of NAFLD) with oral anti diabetic medications, and the fact that in diabetes, any grade of NAFLD induced metabolic and cardiovascular complications, even in lower grades of NAFLD, require pharmacological treatment. Also, the patients included in the current study have been treated with metformin 1500 mg for at least 3 months, and nutrition counseling and physical activity program adjustment have been done to control weight. Therefore, if subjects still have grade 1 NAFLD, adding new agents for therapy is necessary. Hence, the inclusion criteria for the study should be change from the minimum grade 2 NAFLD to grade 1. According to the time of receiving the study ethics code on 14.7.2022, sampling has started after that date. Therefore, it is requested to change the sampling start time to 20.3.2023

Acronym

IRCT registration information

IRCT registration number: **IRCT20220928056051N1**
Registration date: **2022-10-04, 1401/07/12**
Registration timing: **retrospective**

Last update: **2023-04-23, 1402/02/03**

Update count: **1**

Registration date

2022-10-04, 1401/07/12

Registrant information

Name

Laya Hooshmand

Name of organization / entity

Country

Iran (Islamic Republic of)

Phone

+98 44 3345 7286

Email address

hooshmand.l@umsu.ac.ir

Recruitment status**Recruitment complete****Funding source****Expected recruitment start date**

2022-07-14, 1401/04/23

Expected recruitment end date

2023-03-20, 1401/12/29

Actual recruitment start date

2022-07-16, 1401/04/25

Actual recruitment end date

2022-09-26, 1401/07/04

Trial completion date

2023-04-05, 1402/01/16

Scientific title

Comparing the effect of Empagliflozin with Pioglitazone on nonalcoholic fatty liver in diabetic type 2 patients treated with metformin

Public title

Comparing the effect of Empagliflozin with Pioglitazone on nonalcoholic fatty liver

Purpose

Treatment

Inclusion/Exclusion criteria**Inclusion criteria:**

Age between 20 to 75 years Type 2 diabetes A hemoglobin A1C (HbA1c) between 7 and 10 Body mass index (BMI) between 20 to 40 kg/m2 Treated with metformin for at least three months with a minimum dose of 1500 mg daily At least grade 1 of non-alcoholic fatty liver disease (NAFLD)

Exclusion criteria:

Patients receiving drugs that stimulate insulin secretion, or insulin Type 1 diabetes Patients treated with diabetes drugs including sitagliptin and liraglutide Glomerular Filtration Rate (GFR) less than 30 Uncontrolled or aggravated heart disease (class 3 and 4) Liver diseases including autoimmune hepatitis and viral hepatitis Alcohol consumption of more than 140 cc for women and 250 cc for men per week Pregnancy breastfeeding History of recurrent urinary tract infection Bladder Cancer

AgeFrom **20 years** old to **75 years** old**Gender**

Both

Phase

3

Groups that have been masked*No information***Sample size**Target sample size: **60**Actual sample size reached: **60****Randomization (investigator's opinion)**

Randomized

Randomization description

Patients will be divided into two groups using the block randomization method based on generated numbers by Random allocation software. Thus, in this software, first, the number of groups and the total determined sample

size will be entered, and then in the block section, the Block randomization method will be implemented. According to the total sample size (60 patients), 15 blocks of 4 will be used. Patients will be allocated to intervention groups based on generated numbers.

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**

Ethics Committee of Urmia University of Medical Sciences

Street address

Urmia University of Medical Sciences, Resalat Ave, Jahad Blvd., Urmia, Iran.

City

Urmia

Province

West Azarbaijan

Postal code

5714783734

Approval date

2022-07-13, 1401/04/22

Ethics committee reference number

IR.UMSU.REC.1401.180

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**

Liver steatosis score

Timepoint

Before and 6 months after the intervention

Method of measurement

Fibroscan

2

Description

Alanine transaminase (ALT)

Timepoint

Before and 6 months after the intervention

Method of measurement

blood sample

3

Description

Aspartate transaminase (AST)

Timepoint

Before and 6 months after the intervention

Method of measurement

blood sample

4

Description

Alkaline phosphatase (ALKP)

Timepoint

Before and 6 months after the intervention

Method of measurement

blood sample

Secondary outcomes

1

Description

HbA_{1c}

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

2

Description

Cholesterol

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

3

Description

high-density lipoprotein (HDL)

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

4

Description

low-density lipoprotein (LDL)

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

5

Description

triglyceride

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

6

Description

Serum creatinine

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

7

Description

Glomerular filtration rate (GFR)

Timepoint

Before and 6 months after the intervention

Method of measurement

Based on the formula

8

Description

Serum insulin

Timepoint

Before and 6 months after the intervention

Method of measurement

Blood sample

Intervention groups

1

Description

Intervention group: In group one, patients will receive 30 mg pioglitazone daily in addition to the standard treatment (metformin) for 6 months.

Category

Treatment - Drugs

2

Description

Intervention group: in group two, patients will receive 10 mg empagliflozin daily in addition to the standard treatment (metformin) for 6 months.

Category

Treatment - Drugs

Recruitment centers

1

Recruitment center

Name of recruitment center

Urmia Imam Khomeini hospital

Full name of responsible person

Dr. Laya Hooshmand

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity

Oroumia University of Medical Sciences

Full name of responsible person

Dr. Saber Gholizadeh

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Urmia University of Medical Sciences., Resalat street., Jihad Blvd., Urmia, Iran.

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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

Oroumia 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

Oroumia University of Medical Sciences

Full name of responsible person

Dr. Laya Hooshmand

Position

Assistant professor

Latest degree

Subspecialist

Other areas of specialty/work

Internal Medicine

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Person responsible for scientific inquiries

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Sharing plan**Deidentified Individual Participant Data Set (IPD)**

No - There is not a plan to make this available

Justification/reason for indecision/not sharing IPD

Confidentiality of patient information

Study Protocol

No - There is not a plan to make this available

Statistical Analysis Plan

Not applicable

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

Not applicable

Data Dictionary

Not applicable

Title and more details about the data/document

Individual data will not be published and the results will be accessible as a published article.

When the data will become available and for how long

After publishing the article

To whom data/document is available

Researchers

Under which criteria data/document could be used

Not applicable

From where data/document is obtainable

address of the corresponding author:

hooshmand.l@umsu.ac.ir

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

address of the corresponding author:

hooshmand.l@umsu.ac.ir

Comments