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

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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
Age
From **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
HbA1c
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

Street address
Ershad Ave., Modarress Blvd., Imam Khomeini hospital., Urmia., Iran.

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Sponsors / Funding sources

1

Sponsor

Name of organization / entity
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Full name of responsible person
Dr. Saber Gholizadeh

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Urmia University of Medical Sciences., Resalat street., Jahad 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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Ershad Ave., Modarress Blvd., Imam Khomeini hospital., Urmia., Iran.

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Person responsible for updating data

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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