Clinical Trial Protocol
Iranian Registry of Clinical Trials

27 Jul 2026

The comparison of the Empagliflozin effect on nonalcoholic fatty liver in patients with diabetic type 2 with metformin-containing regimens

Protocol summary

Study aim

Assessment of the empagliflozin effect on the non-alcoholic fatty liver of type 2 diabetic patients with metformin-containing regimens

Design

A clinical trial with the parallel control group, an open-label, randomized, phase3, on 60 patients, block randomization was used in SPSS for randomization

Settings and conduct

NAFLD can lead to cardiovascular disease, chronic kidney disease, and increased mortality. In this study, 60 patients in two groups, would be evaluated for the assessment of the empagliflozin effect on the treatment of non-alcoholic fatty liver.

Participants/Inclusion and exclusion criteria

Patients in the age range of 20-75 years with type 2 diabetes and with HbA1C= 6.5-10% and BMI >20 and weight change of less than 10% in the last three months are indicated for inclusion in this study if only they are treated with metformin 1500 mg daily for at least three months as monotherapy and have a definite diagnosis of NAFLD Excluded patients: Type 1 diabetes, treated with other diabetes drugs except for metformin, Hx pancreatitis, or pancreatic-related diseases, ALT more than twice normal upper limits at baseline and eGFR below 45, decompensated heart failure (FC of 3 and 4), other liver diseases including autoimmune and viral hepatitis, alcohol consumption of more than 140 ccs for women and 250 ccs for men per week, pregnant woman or planning a pregnancy, and breastfeeding.

Intervention groups

Group one is metformin according to the instructions and in group two, 10 mg of empagliflozin once daily will be added to the standard treatment and will be re-evaluated within 6 months. Finally, at the end of the study, they undergo an ultrasound and fiber scan to redefine the liver stage.

Main outcome variables

FBS LDL HDL Cholesterol Triglyceride AST ALT ALKP HbA1C CAP score

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. with considering that in the control group, the patients should be on metformin with dose less than 1500 mg per day before entry to the study, and in the intervention group, the patients must have received a minimum dose of 1500 mg metformin for 3 months before enrollment to the study, therefore, it was not possible for using randomization. In exclusion criteria, GFR was corrected to less than 45 ml/min. Due to the lack of difference between the doses of 10 and 25 mg of empagliflozin in the therapeutic effect on NAFLD in diabetic patients, this drug was started for patients with a dose of 10 mg. The dose of 25 mg recorded in the initial version of the clinical trial was changed to 10 mg/day.

Acronym

IRCT registration information

IRCT registration number: **IRCT20220115053717N1**
Registration date: **2022-06-17, 1401/03/27**
Registration timing: **prospective**

Last update: **2023-06-20, 1402/03/30**
Update count: **1**

Registration date

2022-06-17, 1401/03/27

Registrant information

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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

2022-06-19, 1401/03/29

Expected recruitment end date

2022-12-19, 1401/09/28

Actual recruitment start date

2022-07-16, 1401/04/25

Actual recruitment end date

2022-10-03, 1401/07/11

Trial completion date

2023-04-05, 1402/01/16

Scientific title

The comparison of the Empagliflozin effect on nonalcoholic fatty liver in patients with diabetic type 2 with metformin-containing regimens

Public title

Investigating the Empagliflozin effect on nonalcoholic fatty liver in patients with diabetic type 2 with metformin-containing regimens

Purpose

Treatment

Inclusion/Exclusion criteria

Inclusion criteria:

Controlled type 2 Diabetes Mellitus (T2DM) with HbA1C=6.5-10 BMI greater than 20, with the last 3 months loss of weight below 10% treatment with Metformin, 1500mg daily, at least 3 months as monotherapy Statin consumption Definitive diagnosis of NAFLD under the supervision of a Gastroenterology subspecialty at least grade 1 of non-alcoholic fatty liver disease (NAFLD) based on ultrasonography

Exclusion criteria:

Type 1 Diabetes Mellitus (T1DM) Treated with other diabetes medications except for metformin at baseline History of pancreatitis or pancreas related diseases At the beginning of the study ALT more than twice normal upper limits eGFR lower than 45 ml/min Decompensated or untreated Heart Failure (functional class 3 or 4) Other liver diseases include autoimmune hepatitis and viral hepatitis Alcohol consumption more than 140 cc for women and 250 cc for men per week A pregnant woman or someone who is planning a pregnancy breastfeeding

Age

From **20 years** old to **75 years** old

Gender

Both

Phase

2-3

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 intervention or control 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 (60 patients), and then in the block section, the Block randomization method will be implemented. Patients will be allocated to groups based on generated numbers. Random Allocation Software version 1.0.0 has been developed by Mr. Saghaei, MD. department of anesthesia, Isfahan University of Medical Sciences, Isfahan, Iran.

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 Committees of Urmia University of Medical Sciences

Street address

Orjhans Street, Resalat Blvd, Urmia

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Province

West Azarbaijan

Postal code

571478334

Approval date

2022-01-02, 1400/10/12

Ethics committee reference number

IR.UMSU.HIMAM.REC.1400.010

Health conditions studied

1

Description of health condition studied

Type 2 diabetic patients with nonalcoholic fatty liver disease

ICD-10 code

5A11, DB92

ICD-10 code description

type 2 diabetes mellitus, nonalcoholic fatty liver disease

Primary outcomes

1

Description
CAP score or STAGE determination index of steatohepatitis that is measured and evaluated by Fibroscan
Timepoint
at the beginning and the end of study of(after 6 months of treatment)
Method of measurement
Fibroscan device and its analysis by an experienced unit

Secondary outcomes

empty

Intervention groups

1

Description
Control group: Treatment with metformin according to standard instructions and methods
Category
Treatment - Drugs

2

Description
Intervention group: Treatment with Empagliflozin 25 mg once in the morning added to the standard treatment (Metformin)
Category
Treatment - Drugs

Recruitment centers

1

Recruitment center
Name of recruitment center
Imam Khomeini University Hospital
Full name of responsible person
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Sponsors / Funding sources

1

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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
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Associate professor
Latest degree
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Person responsible for updating data

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Sharing plan

Deidentified Individual Participant Data Set (IPD)
Yes - There is a plan to make this available
Study Protocol
No - There is not a plan to make this available
Statistical Analysis Plan
No - There is not 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
Not applicable
Data Dictionary
Not applicable
Title and more details about the data/document
The data that support the findings of this study are available from the corresponding author, L. H., upon reasonable request.
When the data will become available and for how long
The data that support the findings of this study are available from the corresponding author, L. H., upon reasonable request.
To whom data/document is available
The data that support the findings of this study are available from the corresponding author, L. H., upon reasonable request.
Under which criteria data/document could be used
The data that support the findings of this study are available from the corresponding author, L. H., upon reasonable request.
From where data/document is obtainable
The data that support the findings of this study are available from the corresponding author, L. H., upon reasonable request.
What processes are involved for a request to access data/document
The data that support the findings of this study are available from the corresponding author, L. H., upon reasonable request.
Comments