

# Clinical Trial Protocol

## Iranian Registry of Clinical Trials

10 Jun 2026

### **Study the effect of ezetimibe along with metformin on changes in PPAR- $\gamma$ and adiponectin expression, serum levels of liver enzymes, degree of hepatic steatosis, blood glycemic and lipids parameters in non-alcoholic fatty liver grade 2 patients suffering from diabetes: clinical trial**

#### **Protocol summary**

##### **Study aim**

Comparison of metformin alone and combination of metformin with ezetimibe on PPAR- $\gamma$  and adiponectin gene expression ,serum level of medical enzymes , degree of dietary steatosis , glycemic and blood lipid parameters in non- alcoholic fatty liver disease in grade 2 patients

##### **Design**

Clinical trial with 2 control and intervention groups, parallel groups, randomized, phase 4 on two groups of 80 people.

##### **Settings and conduct**

The participants in this project will be entered by the endocrinology and metabolism specialist from Nikbakht Clinic in Isfahan in 2023 based on the entry criteria of the study. Serum lipid profile (HDL and LDL-Cholesterol, Triglycerides) using commercial enzymatic method, serum level of GGT, AST and ALT by calorimetric method, insulin level by Cobas e411device, and interleukin 6 level by Imolite device method will be measured. Also serum MDA and TAC will be assayed using calorimetric method. Separation of mononuclear cells by PBMC and extraction of RNA and cDNA synthesis will be done with Fermantase kits. Gene expression of PPAR- $\gamma$  and adiponectin will be assayed using Real time PCR method.

##### **Participants/Inclusion and exclusion criteria**

Diabetic patients with NAFLD

##### **Intervention groups**

The use of ezetimibe and metformin in the treatment of grade 2 non- alcoholic fatty liver patients with diabetes. The intervention group receives a daily dose of 10 mg ezetimibe from Hakim pharmaceutical company and between 500-2500 mg metformin tablets from Raha pharmaceutical company and the control group will take 500-2500 mg metformin tablets daily for 6 months.

##### **Main outcome variables**

In this study , the expression of adiponectin and PPAR- $\gamma$  and the level of liver enzymes, the degree of steatosis, glycemic indices and lipid profile as the primary outcomes, as well as the serum levels of TAC, MDA and interleukin 6 and anthropometric indices will be considered as secondary outcomes

#### **General information**

##### **Reason for update**

##### **Acronym**

##### **IRCT registration information**

IRCT registration number: **IRCT20090305001745N3**

Registration date: **2023-12-03, 1402/09/12**

Registration timing: **prospective**

Last update: **2023-12-03, 1402/09/12**

Update count: **0**

##### **Registration date**

2023-12-03, 1402/09/12

##### **Registrant information**

##### **Name**

Mohamad Taghi Goodarzi

##### **Name of organization / entity**

Hamadan University of Medical Sciences

##### **Country**

Iran (Islamic Republic of)

##### **Phone**

+98 81 3838 0462

##### **Email address**

mt.goodarzi@umsha.ac.ir

##### **Recruitment status**

**Recruitment complete**

##### **Funding source**

**Expected recruitment start date**

2023-12-06, 1402/09/15

**Expected recruitment end date**

2024-06-04, 1403/03/15

**Actual recruitment start date**

empty

**Actual recruitment end date**

empty

**Trial completion date**

empty

**Scientific title**

Study the effect of ezetimibe along with metformin on changes in PPAR- $\gamma$  and adiponectin expression, serum levels of liver enzymes, degree of hepatic steatosis, blood glycemic and lipids parameters in non-alcoholic fatty liver grade 2 patients suffering from diabetes: clinical trial

**Public title**

A comparative study of the use of metformin and ezetimibe compared to the use of metformin in the treatment of non-alcoholic fatty liver disease

**Purpose**

Treatment

**Inclusion/Exclusion criteria****Inclusion criteria:**

Type 2 diabetes is known ( under treatment) At least one year has passed since their diabetes NAFLD grade 2 or 3 has been diagnosed by ultrasound All patients should undergo non -pharmacological life style modification treatment

**Exclusion criteria:**

Newly diagnosed subjects Type 1 diabetes Receiving only insulin treatment Drug intolerance disorders Lack of consent to continue treatment Diagnosis of type 1 NAFLD Having a weight loss of more than 5 % Having Infectious diseases , cancer, allergy and immune - based diseases Smoking and alcohol consumption Appetite disorders such as anorexia or overeating Treatment with amphetamine, cyproheptadine, phenothiazine, appetite suppressants or appetite stimulants Chronic viral hepatitis (HBV-HCV-HDV), drug-induced liver disease , Wilson's disease , hereditary deficiency of antitrypsin 1, idiopathic hemochromatosis, history of complications from liver diseases including ascites , encephalopathy or variceal bleeding Uncontrolled cardiovascular or respiratory disease , active malignancy or active and chronic infections The use of agents such as vitamin E- omega 3 fatty acids or drugs with evidence of their effect on NAFLD (pioglitazon , GLP 1analog , dipeptidyl peptidase inhibitors IV ,ursodeoxycholic acid) Pregnancy or breastfeeding Use of corticosteroids Taking herbal medicines whose effect on fatty liver has been proven Taking any nutritional supplements in the last 3 months

**Age**From **30 years** old to **60 years** old**Gender**

Both

**Phase**

3

**Groups that have been masked***No information***Sample size**Target sample size: **80****Randomization (investigator's opinion)**

Randomized

**Randomization description**

Simple randomization using individual method by the Endocrinologist. The patients will be divided into groups according the number of their registration in clinic: odd numbers in control group and even numbers in intervention group.

**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 Islamic Azad University of Shahrood

**Street address**

Daneshgah Blvd.

**City**

Shahrood

**Province**

Semnan

**Postal code**

3614871151

**Approval date**

2023-09-07, 1402/06/16

**Ethics committee reference number**

IR.IAU.SHAHROOD.REC.1402.043

**Health conditions studied****1****Description of health condition studied**

Diabetes

**ICD-10 code**

E11.6

**ICD-10 code description**

Type 2 diabetes mellitus with other specified complications

**Primary outcomes****1****Description**

Liver steatosis

**Timepoint**

At the beginning of intervention and 6 months after that date.

**Method of measurement**

Sonography

**2**

**Description**

Adiponectin gene expression

**Timepoint**

At the beginning of intervention and 6 months after that date

**Method of measurement**

Real time PCR

**3**

**Description**

PPAR- gamma Gene expression

**Timepoint**

At the beginning of intervention and 6 months after that

**Method of measurement**

Real time PCR

**4**

**Description**

Activity of liver enzymes in serum

**Timepoint**

At the beginning of intervention and 6 months after that date

**Method of measurement**

Spectrophotometry

**5**

**Description**

Patients lipid profile

**Timepoint**

At the beginning of intervention and 6 months after that date

**Method of measurement**

Autoanalyzer (Spectrophotometry)

**6**

**Description**

Serum Level of IL-6

**Timepoint**

At the beginning of intervention and 6 months after that date

**Method of measurement**

Enzyme Immunoassay

**7**

**Description**

Serum Level of Malone- di-aldehyde

**Timepoint**

At the beginning of intervention and 6 months after that date

**Method of measurement**

Spectrophotometry

**Secondary outcomes**

**1**

**Description**

Total Antioxidant Capacity

**Timepoint**

At the beginning of intervention and 6 months after that date.

**Method of measurement**

Spectrophotometry

**2**

**Description**

Fasting blood glucose

**Timepoint**

At the beginning of intervention and 6 months after that date.

**Method of measurement**

Autoanalyzer

**3**

**Description**

2 hours post prandial glucose

**Timepoint**

At the beginning of intervention and 6 months after that date.

**Method of measurement**

Autoanalyzer

**4**

**Description**

Glycated hemoglobin (HbA1c)

**Timepoint**

At the beginning of intervention and 6 months after that date.

**Method of measurement**

Spectrophotometry

**5**

**Description**

Insulin Resistance Index ( HOMA-IR)

**Timepoint**

At the beginning of intervention and 6 months after that date.

**Method of measurement**

Calculation according to the related formula

**Intervention groups**

**1**

**Description**

Intervention group: grade 2 non- alcoholic fatty liver patients with diabetes receives a daily dose of 10 mg

ezetimibe (Hakim pharmaceutical company )and between 500-2500 mg metformin tablets (Raha pharmaceutical company) for 6 months.

**Category**

Treatment - Drugs

**2****Description**

Control group: grade 2 non- alcoholic fatty liver patients with diabetes receives 500-2500 mg metformin tablets (Raha pharmaceutical company) for 6 months.

**Category**

Treatment - Drugs

**Recruitment centers****1****Recruitment center****Name of recruitment center**

Nikbakht Clinic

**Full name of responsible person**

Mohammad Reza Mirzaei

**Street address**

Nikbakht Clinic No 48, West Nikbakht St, Chaharbagh Bala St.

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mohamadmiraie@yahoo.com

**Web page address**

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**Sponsors / Funding sources****1****Sponsor****Name of organization / entity**

Islamic Azad University of Shahrood

**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?**

No

**Title of funding source**

There is no financial support for this project. It will be carried out in personal expenses.

**Proportion provided by this source**

100

**Public or private sector**

Private

**Domestic or foreign origin**

Domestic

**Category of foreign source of funding**

empty

**Country of origin****Type of organization providing the funding**

Persons

**Person responsible for general inquiries****Contact****Name of organization / entity**

Islamic Azad University of Shahrood

**Full name of responsible person**

Mohammad Taghi Goodarzi

**Position**

Professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Biochemistry

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**Person responsible for scientific inquiries****Contact****Name of organization / entity**

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**Full name of responsible person**

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**Position**

Professor

**Latest degree**

Ph.D.

**Other areas of specialty/work**

Biochemistry

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## Person responsible for updating data

**Contact**

**Name of organization / entity**

Islamic Azad University of Shahrood

**Full name of responsible person**

Asieh Maseli

**Position**

Ph.D. candidate

**Latest degree**

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**Other areas of specialty/work**

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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**

Not applicable