# Clinical Trial Protocol
# Iranian Registry of Clinical Trials

07 Nov 2026

## Comparison of the effect of Empagliflozin and Sitaglipin, as add on to metformin on Fetuin-A serum level and insulin resistance in patient with type 2 diabetes

## Protocol summary

**Study aim**

Comparison of the effect of Empagliflozin and Sitaglipin, as add on to metformin on Fetuin-A serum level and insulin resistance in patient with type 2 diabetes

**Design**

A single-blind, randomized, parallel-group clinical trial of 74 patients using stratified permuted block randomization.

**Settings and conduct**

A single-blind randomized trial on 74 type 2 diabetes patients at Tohid Diabetes Clinic in Sanandaj. Patients will be randomly allocated (using permuted block stratified randomization) to either empagliflozin + metformin or sitagliptin + metformin groups. Outcome assessors, statistical analysts, and the safety committee will be blinded

**Participants/Inclusion and exclusion criteria**

Inclusion Criteria: Iranians with T2DM (6mo-10yrs), BMI more than 25, no recent acute illness, on metformin with HbA1c 7.5-8.5%. Exclusion Criteria: Severe diabetes complications, cognitive disorders, BP more than or equal to 180/110, hemolytic anemia, hemoglobinopathies, or recent diabetes medication changes.

**Intervention groups**

This single-blind clinical trial compares the efficacy of two active treatment regimens in patients with type 2 diabetes. In the first group, patients will receive a fixed dose of empagliflozin 10 mg daily along with metformin at an adjusted dose between 1000-2000 mg daily. In the second group, patients will receive sitagliptin at a renal function-adjusted dose (100 mg daily for eGFR≥50, 50 mg for eGFR 30-49, and 25 mg for eGFR<30) along with metformin following the same dosing protocol as the first group. The treatment protocol includes gradual initiation of metformin starting from 500 mg with weekly dose escalation based on patient tolerance, and metformin will be discontinued in cases of reduced kidney function (eGFR<30).

**Main outcome variables**

Primary: -Serum fetuin-A level, -Insulin resistance. Secondary: -Fasting blood glucose, -Hemoglobin A1c, -lipid profile, -BMI.

## General information

**Reason for update**

**Acronym**

**IRCT registration information**

IRCT registration number: **IRCT20160625028627N3**
Registration date: **2025-05-27, 1404/03/06**
Registration timing: **prospective**

Last update: **2025-05-27, 1404/03/06**
Update count: **0**

**Registration date**

2025-05-27, 1404/03/06

**Registrant information**

**Name**
Golnaz Azami
**Name of organization / entity**
Medical University of Ilam
**Country**
Iran (Islamic Republic of)
**Phone**
009884133336766 & 0060389400975
**Email address**
gs41829@student.upm.edu.my

**Recruitment status**

**Recruitment complete**

**Funding source**

**Expected recruitment start date**

2025-06-20, 1404/03/30

**Expected recruitment end date**
2025-09-21, 1404/06/30
**Actual recruitment start date**
empty
**Actual recruitment end date**
empty
**Trial completion date**
empty

**Scientific title**
Comparison of the effect of Empagliflozin and Sitaglipin, as add on to metformin on Fetuin-A serum level and insulin resistance in patient with type 2 diabetes

**Public title**
Comparison of the effect of Empagliflozin and Sitaglipin, as add on to metformin on diabetes treatment
**Purpose**
Treatment
**Inclusion/Exclusion criteria**
**Inclusion criteria:**
Iranian nationality Diagnosed with type 2 diabetes for a minimum of 6 months and a maximum of 10 years Body mass index greater than or equal to 25 No acute illness in the past 6 months Patients must have been on stable-dose metformin monotherapy for the past 3 months, yet their blood glucose remains uncontrolled (outside target range), demonstrating metformin resistance, with hemoglobin A1c levels between 7.5-8.5%
**Exclusion criteria:**
Development of type 2 diabetes complications that disrupt care (e.g., blindness, dialysis, severe stroke) Medical history of cognitive disorders (e.g., dementia, Alzheimer's) Uncontrolled hypertension more than 180/110 millimeters of mercury Hemolytic anemia Hemoglobinopathies Any change in type/dose of prescribed diabetes medications during the 3-month study period Patients with a history of fatty liver disease Concurrent use of antioxidant or anti-inflammatory drugs Patients with thyroid disorders
**Age**
From **18 years** old
**Gender**
Both

**Phase**
2
**Groups that have been masked**

- Outcome assessor
- Data analyser
- Data and Safety Monitoring Board

**Sample size**
Target sample size: **74**
**Randomization (investigator's opinion)**
Randomized
**Randomization description**
Method of randomization: Stratified permuted block randomization (block sizes: 4, 6) to ensure balanced allocation. Unit of randomization: Individual participants. Randomization strata: age (less than 50 years versus age greater than or equal to 50 years), sex, and duration of diabetes (greater than or equal to 5 years versus less than 5 years). Randomization tool: Computer-generated random sequences (statistical software), with separate sequences per stratum. Random sequence generation: Software-produced sequences ensured unpredictability within blocks. Allocation concealment: Maintained via an independent researcher using sequentially numbered, opaque envelopes or a secure electronic system.
**Blinding (investigator's opinion)**
Single blinded
**Blinding description**
In this study, three main groups including outcome assessors (who measure outcomes without knowledge of group allocation), data analysts (who do not have access to grouping information), and the Data and Safety Monitoring Board (who only access allocation information when necessary) were kept blinded to participant allocation to prevent bias. Evaluations were based on coded data and analyses were performed independently.
**Placebo**
Not used
**Assignment**
Parallel
**Other design features**

## Secondary Ids

empty

## Ethics committees

### 1

**Ethics committee**
**Name of ethics committee**
Ethic committee of Kurdistan University of Medical Sciences
**Street address**
Pasdaran Boulevard, Kurdistan University of Medical Sciences, Sanandaj, Iran
**City**
Sanandaj
**Province**
Kurdistan
**Postal code**
6617913446
**Approval date**
2025-02-16, 1403/11/28
**Ethics committee reference number**
IR.MUK.REC.1403.324

## Health conditions studied

### 1

**Description of health condition studied**
Type 2 diabetes
**ICD-10 code**
E11
**ICD-10 code description**
Type 2 diabetes mellitus

## Primary outcomes

### 1

**Description**
Mean serum fetuin-A level
**Timepoint**
Serum fetuin-A levels will be measured before the intervention and at week 12.
**Method of measurement**
The blood test using the ELISA method

### 2

**Description**
Mean change in insulin resistance
**Timepoint**
Mean change in insulin resistance will be measured before the intervention and at week 12.
**Method of measurement**
Blood test using ELISA kit (HOMA-IR index)

## Secondary outcomes

### 1

**Description**
Mean change in fasting blood glucose levels
**Timepoint**
Mean change in fasting blood glucose levels will be measured before the intervention and week 12 post-intervention.
**Method of measurement**
The blood test will be performed using a glucometer

### 2

**Description**
Mean change in glycated hemoglobin
**Timepoint**
Mean change in glycated hemoglobin will be measured before the intervention and 12 weeks post-intervention
**Method of measurement**
Blood test-measured by high-performance liquid chromatography/HPLC

### 3

**Description**
Mean change in serum triglyceride levels
**Timepoint**
Mean change in serum triglyceride levels will be measured before the intervention and 12 weeks post-intervention
**Method of measurement**
Blood test- measured by enzymatic method

### 4

**Description**
Mean change in serum total cholesterol levels
**Timepoint**
Mean change in serum total cholesterol levels will be measured before the intervention and 12 weeks post-intervention
**Method of measurement**
Blood test- measured by enzymatic method

### 5

**Description**
Mean change in serum HDL levels
**Timepoint**
Mean change in serum HDL levels will be measured before the intervention and 12 weeks post-intervention
**Method of measurement**
Blood test- measured by enzymatic method

### 6

**Description**
Mean change in serum LDL levels
**Timepoint**
Mean change in serum LDL levels will be measured before the intervention and 12 weeks post-intervention
**Method of measurement**
Blood test- measured by enzymatic method

### 7

**Description**
Mean change in body mass index (kg/m²)
**Timepoint**
Mean change in body mass index will be measured before the intervention and 12 weeks post-intervention
**Method of measurement**
Measurements will be performed by trained staff using calibrated digital scales (accuracy 0.1 kg) and standard stadiometers (accuracy 0.5 cm).

## Intervention groups

### 1

**Description**
Intervention group 1 (Empagliflozin + Metformin Group):In the first group, patients with type 2 diabetes who failed to achieve adequate glycemic control (HbA1c 7.5-8.5%) despite at least 3 months of metformin monotherapy (at a fixed dose) received combination therapy with empagliflozin and metformin. Empagliflozin was administered at a fixed dose of 10 mg once daily. Metformin was initiated at 500 mg daily and gradually titrated (with weekly 500 mg increments) up to a maximum dose of 2000 mg daily. Dose escalation was based on patient tolerance and therapeutic response. Renal function (eGFR) was assessed in all patients before treatment initiation and throughout the study, and metformin was discontinued if eGFR fell below 30 mL/min/1.73m².
**Category**
Treatment - Drugs

### 2

**Description**

Intervention group 2 (Sitagliptin + Metformin Group):In the second group, patients with similar characteristics (uncontrolled type 2 diabetes with metformin monotherapy and HbA1c 7.5-8.5%) received combination therapy with sitagliptin and metformin. Sitagliptin dosage was adjusted based on renal function: 100 mg daily for eGFR≥50, 50 mg daily for eGFR 30-49, and 25 mg daily for eGFR<30. The metformin administration protocol in this group was identical to the first group (starting at 500 mg with gradual increase up to 2000 mg daily). All patients underwent renal function assessment before treatment initiation, and drug dosages were individually adjusted according to clinical and laboratory parameters. Metformin was discontinued if renal function declined below 30 mL/min/1.73m².

**Category**
Treatment - Drugs

## Recruitment centers

**1**

**Recruitment center**

**Name of recruitment center**
The specialized diabetes clinic located at Tohid Hospital & Medical Training Center, Sanandaj

**Full name of responsible person**
Dr. Golnaz Azami

**Street address**
Gariyashan St., Basij Sq., Tohid Hospital & Medical Training Center

**City**
Sanandaj

**Province**
Kurdistan

**Postal code**
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golnaz.azami64@gmail.com

## Sponsors / Funding sources

**1**

**Sponsor**

**Name of organization / entity**
Sanandaj University of Medical Sciences

**Full name of responsible person**
Dr. Afshin Maleki

**Street address**
Pasdaran Boulevard, Kurdistan University of Medical Sciences, Sanandaj, Iran

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**Province**
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**Email**
info@muk.ac.ir

**Web page address**
https://www.muk.ac.ir/Page?pageId=477

**Grant name**

**Grant code / Reference number**

**Is the source of funding the same sponsor organization/entity?**
Yes

**Title of funding source**
Sanandaj 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**
Sanandaj University of Medical Sciences

**Full name of responsible person**
Dr. Golnaz Azami

**Position**
Assistant Professor and Faculty Member, Kurdistan University of Medical Sciences

**Latest degree**
Ph.D.

**Other areas of specialty/work**
Nursery

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## Person responsible for scientific inquiries

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## Person responsible for updating data

**Contact**
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Sanandaj University of Medical Sciences
**Full name of responsible person**
Dr. Golnaz Azami
**Position**
Assistant Professor and Faculty Member, Kurdistan University of Medical Sciences
**Latest degree**
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**Other areas of specialty/work**
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## Sharing plan

**Deidentified Individual Participant Data Set (IPD)**
Yes - There is 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**
Yes - There is 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
**Title and more details about the data/document**
The fully anonymized participant data will be shareable upon reasonable request after study completion. The shareable materials include the following: The dataset will include non-identifiable clinical parameters such as HbA1c, blood pressure, and lipid profiles. It should be noted that all personally identifiable information including names, IDs, and contact details will be permanently removed. In the documentation section, the study protocol in both Farsi and English, data collection forms as blank templates, and educational materials including video scripts and booklet content will be made available. The access conditions for this data are such that six months after study publication, the data will become accessible. Requesters must comply with the following requirements: a) Submission of a formal research proposal b) Signing a data use agreement that prohibits re-identification c) Proper source attribution in their publications
**When the data will become available and for how long**
Data will be available 6 months post-publication.
**To whom data/document is available**
The study data and documents will be accessible to both of the following groups: A) Academic researchers: University faculty members, Research institute scientists, Graduate students (with supervisor approval). B) Industry/clinical professionals: Practicing physicians and nurses, Pharmaceutical/medical device specialists, Research & Develpment specialists in health-related companies.
**Under which criteria data/document could be used**
Access to de-identified data and study documents is subject to the following requirements: a) General Conditions: Submission of formal request including research objectives, analysis plan and timeline, Approval by the ethics committee of requester's institution, Signed limited data use agreement. b) Analytical Restrictions: Any statistical analysis is permitted provided it doesn't enable indirect identification, Subgroup comparisons require minimum 10 cases per group, Machine learning applications need separate approval. c) Usage Permissions: Permitted for academic research and therapeutic protocol development, Commercial use requires separate licensing agreement, Educational materials may be redistributed with proper attribution. d) Oversight Mechanisms: Mandatory progress reports every 6 months, Periodic audits by independent data monitor, Data deletion commitment after project completion.
**From where data/document is obtainable**
Interested parties may submit their requests for study data and documentation to the following email address: golnaz.azami64@gmail.com
**What processes are involved for a request to access data/document**
Request Procedure: Formal Request Submission:

Complete request form (if applicable), Email to golnaz.azami64@gmail.com with clear subject. Attach: -Research proposal, -Ethics approval, -Affiliation documents. *Initial Review (3-5 business days): -Document completeness check, -Research objectives alignment assessment, *Technical Evaluation (7-10 business days): -Analysis plan review by technical team, -Access level determination, -De-identified data preparation. *Agreement Finalization (5-7 business days): -NDA signing, -Usage terms confirmation. -Cost determination (if applicable). *Data Delivery (2-3 business days post-agreement): -Secure platform transfer, -User guide provision, -Analysis restrictions specification, Total Processing Time: 15-25 business days (depending on request complexity).

**Comments**