

Effect of SGLT-2 inhibitors on arterial stiffness in a real-world setting

Submission date 19/10/2021	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 19/10/2021	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 17/11/2023	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Patients with type 2 diabetes are at a higher risk for cardiovascular (heart) disease. Arterial stiffness is a marker for cardiovascular disease development. Therefore, the aim of this study is to determine the effect of two different sodium-glucose co-transporter-2 (SGLT-2) inhibitors on arterial stiffness in patients with type 2 diabetes.

Who can participate?

Patients aged 18-75 years old with type 2 diabetes who are starting treatment with an SGLT-2 inhibitor

What does the study involve?

Patients will be evaluated to record demographics, body measurements, medical history and medication use. Blood samples will be taken for testing. All patients will perform a 24-hour urine collection and their blood pressure will be recorded. Finally, all patients will undergo ambulatory blood pressure monitoring with a monitoring device. A follow-up visit is planned for 6 months after starting treatment with an SGLT-2 inhibitor.

What are the possible benefits and risks of participating?

The potential benefits for the patient include blood sugar control and cardio-renal (heart and kidney) benefits. There are no risks expected.

Where is the study run from?

Aristotle University of Thessaloniki (Greece)

When is the study starting and how long is it expected to run for?

April 2019 to May 2022

Who is funding the study?

Investigator initiated and funded

Who is the main contact?

Dr Dimitrios Patoulas

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

EudraCT/CTIS number

Nil known

IRAS number

ClinicalTrials.gov number

Nil known

Secondary identifying numbers

Nil known

Study information

Scientific Title

Effect of SGLT-2 inhibitors on ambulatory arterial stiffness indices in patients with type 2 diabetes mellitus

Study objectives

SGLT-2 inhibitor treatment decreases ambulatory arterial stiffness in patients with type 2 diabetes mellitus.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 17/07/2019, Ethics Committee of the School of Medicine, Aristotle University of Thessaloniki (University Campus of Thessaloniki, Thessaloniki, 54 124, Greece; +30 (0) 2310999338; bioethics@med.auth.gr), ref: 4/17.7.2019

Study design

Single-center single-arm observational study

Primary study design

Observational

Secondary study design

Cohort study

Study setting(s)

Other

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Arterial stiffness in patients with type 2 diabetes mellitus

Interventions

Enrolled participants will be initiated either to dapagliflozin 10 mg or empagliflozin 10 or 25 mg once daily (oral route) for 24 weeks (6 months), according to the treating physician's discretion, as added to previously stable antidiabetic regimen.

Patients will be initially evaluated regarding their potential inclusion in the study, according to the prespecified eligibility criteria. Eligible patients will provide the investigators with written informed consent, after a meticulous explanation of the study procedures.

These patients are instructed to visit the center on a scheduled morning after a 12-h period of fasting. A study investigator will record baseline demographics, anthropometric parameters, medical history and concomitant medication. Blood samples will be taken in order to determine glycated hemoglobin, hematocrit, hemoglobin, serum creatinine, estimated glomerular filtration rate, serum sodium, serum uric acid and CRP levels. All patients will be instructed to perform a 24 h urine collection ending on the morning of the baseline evaluation to measure urine albumin. Office blood pressure will be recorded with a validated oscillometric device and a cuff of appropriate size with the patient sitting for at least 10 min and with three measurements per occasion taken 2 min apart. Finally, all patients will undergo ambulatory blood pressure monitoring (ABPM) with the Mobil-O-Graph® 24h PWA device (IEM GmbH). Blood pressure monitoring will be performed every 20 minutes during the daytime (7:00 to 23:00) and every 30 minutes during the nighttime (23:00 to 7:00). Measurements will be used for the analysis if >70% of recordings were valid. Central hemodynamics and arterial stiffness indices will be also recorded with the Mobil-O-Graph® 24h PWA device, as previously described. The augmentation index will be calculated as the augmentation pressure, which is the pressure of the second systolic peak minus the pressure at the inflection point, expressed as a percentage of the pulse

pressure and normalized for a HR of 75 bpm (Aix@HR75). A follow-up visit is planned to be performed 6 months after the initiation of an SGLT-2 inhibitor.

Intervention Type

Drug

Phase

Not Applicable

Drug/device/biological/vaccine name(s)

Empagliflozin, dapagliflozin

Primary outcome measure

Ambulatory pulse wave velocity (PWV) measured using the Mobilograph device at baseline and 6 months

Secondary outcome measures

1. Ambulatory central pulse pressure measured using the Mobilograph device at baseline and after 6 months
2. Ambulatory augmentation index measured using the Mobilograph device at baseline and after 6 months
3. Rest parameters measured using the Mobilograph device at baseline and after 6 months

Overall study start date

01/04/2019

Completion date

01/05/2022

Eligibility**Key inclusion criteria**

1. Male or female
2. Aged 18-75 years old
3. Established diagnosis of type 2 diabetes mellitus (≥ 12 months)
4. HbA1c values 6.5 – 10.0%
5. Stable antidiabetic and antihypertensive treatment over the last 6 months
6. Indication for the initiation or addition of new antidiabetic therapy with an SGLT-2 inhibitor according to the treating physician's discretion
7. Written informed consent

Participant type(s)

Patient

Age group

Adult

Lower age limit

18 Years

Upper age limit

75 Years

Sex

Both

Target number of participants

60

Total final enrolment

55

Key exclusion criteria

1. Type 1 diabetes mellitus
2. History of a serious adverse reaction to an SGLT-2 inhibitor
3. Renal dysfunction (estimated glomerular filtration rate <45 ml/min/1.73 m²)
4. Body mass index greater than 45 kg/m²
5. Uncontrolled hypertension despite optimal treatment (blood pressure $\geq 180/110$ mmHg)
6. Liver dysfunction
7. Recent revascularization procedure or admission to hospital due to worsening of pre-existing heart failure (during the last 3 months)
8. Recent hospitalization due to diabetic ketoacidosis (during the last 3 months)
9. Alcohol or illicit drug intake
10. Pregnancy, possible pregnancy or breastfeeding
11. Participation of the patient in another clinical study

Date of first enrolment

01/08/2019

Date of final enrolment

01/12/2021

Locations**Countries of recruitment**

Greece

Study participating centre

Aristotle University of Thessaloniki

Diabetes Centre

Second Propedeutic Department of Internal Medicine

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Sponsor information

Organisation

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Sponsor details

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Sponsor type

University/education

Website

<https://www.auth.gr/en>

ROR

<https://ror.org/02j61yw88>

Funder(s)**Funder type**

Other

Funder Name

Investigator initiated and funded

Results and Publications**Publication and dissemination plan**

Planned publication in a high-impact peer-reviewed journal.

Intention to publish date

31/12/2021

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Interim results article	Sub-analysis	16/11/2021	15/02/2022	Yes	No
Results article		27/08/2022	29/09/2022	Yes	No
Other publications		01/07/2022	17/11/2023	Yes	No