ISRCTN88851713 https://doi.org/10.1186/ISRCTN88851713

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

Submission date	Recruitment status	[_] Prospectively registered
19/10/2021	No longer recruiting	[_] Protocol
Registration date	**Overall study status**	[_] Statistical analysis plan
19/10/2021	Completed	[X] Results
Last Edited	**Condition category**	[_] Individual participant data
17/11/2023	Circulatory System	

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 Patoulias
patoulias@auth.gr

Contact information

Type(s)
Scientific

Contact name
Dr Dimitrios Patoulias

Contact details
Konstantinoupoleos 49
Theesaloniki
Greece
54642
+30 (0)6946900777
patoulias@auth.gr

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
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

Study type(s)
Treatment

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

Key secondary outcome(s))
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

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

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
75 years

Sex
All

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 m^2)
4. Body mass index greater than 45 kg/m^2
5. Uncontrolled hypertension despite optimal treatment (blood pressure ≥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
Konstantinoupoleos 49
Thessaloniki
Greece
54642

Sponsor information

Organisation
Aristotle University of Thessaloniki

ROR
https://ror.org/02j61yw88

Funder(s)

Funder type
Other

Funder Name

Investigator initiated and funded

Results and Publications

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?
Results article		27/08/2022	29/09/2022	Yes	No
Interim results article		16/11/2021	15/02/2022	Yes	No
Other publications	Sub-analysis	01/07/2022	17/11/2023	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes