

# Sotagliflozin in patients with heart failure symptoms and type 1 diabetes

<b>Submission date</b> 23/01/2024	<b>Recruitment status</b> Recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 12/03/2024	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 01/07/2025	<b>Condition category</b> Nutritional, Metabolic, Endocrine	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

People with type 1 diabetes sometimes develop heart failure which can cause symptoms like breathlessness, tiredness or ankle swelling, reduced quality of life and lead to being admitted to hospital or suffering potentially fatal consequences. This trial is investigating if a tablet called sotagliflozin can improve quality of life in people with type 1 diabetes and heart failure. In addition, this trial will also assess the safety and tolerability of sotagliflozin in this population. In previous trials that included people with type 2 diabetes and heart failure sotagliflozin was shown to improve patients' symptoms of heart failure, quality of life and reduce the chance of people with heart failure being admitted to hospital or dying. However, people with type 1 diabetes and heart failure were not included in these trials meaning that we do not know if these benefits also apply to this population.

### Who can participate?

People aged 18 to 85 years with type 1 diabetes and heart failure symptoms

### What does the study involve?

This trial will compare the health and quality of life of participants who take sotagliflozin tablets with participants who take placebo tablets, which is a dummy tablet that looks the same as sotagliflozin. Participants will be randomly allocated to one of two groups (i.e. one taking sotagliflozin and the other the placebo) and both the medical team and participants will not know in which group each participant is until the end of the study. Participants will be in the trial for about 6 months and will be given sotagliflozin or placebo tablets to take 1 per day for 4 months. The trial is expected to run for a total of 26 months.

### What are the possible benefits and risks of participating?

By taking part you are contributing to medical science. The results may help other people in the future. If we find that sotagliflozin does make people with type 1 diabetes and heart failure feel better, then we might use sotagliflozin to treat people like you in future.

You'll be monitored closely during the trial by the trial team. If any of the investigations and assessments reveal any new clinically significant abnormality, we'll tell you and either discuss this with your GP (with your consent) or refer you to a specialist clinic at the hospital. We'll also be reviewing your current treatment for diabetes and heart failure and may be able to help

improve this.

If sotagliflozin has the same effect as SGLT inhibitors have in people with type 2 diabetes or people without diabetes, and you are allocated to take sotagliflozin in this trial you might notice that your heart failure symptoms improve. You may also find that your glucose levels improve.

**Diabetic ketoacidosis (DKA):** SGLT2i therapy in type 1 diabetes is associated with an increased risk (~3%) of DKA. Participants will be asked to perform capillary ketone testing 4 times per day 3 days before and 3 days after initiation of active drug/placebo and 2 hours after changing each insulin giving set for those on insulin pump therapy as described earlier. They will also be given advice on ketone recording when unwell.

**Hypoglycaemia:** there is a small increased risk of severe hypoglycaemia with sotagliflozin. Once randomisation is complete, participants with a HbA1c <58mmol/l will have a 10% insulin dose reduction prior to taking their first dose of sotagliflozin/placebo to reduce the risk of severe hypoglycaemia. Further dose adjustments will be given to all participants throughout the trial if required.

All patients with type 1 diabetes will routinely be given advice about DKA and hypoglycaemia within their standard care. This prior knowledge will be supplemented with additional education around preventing, recognising and treating DKA and hypoglycaemia and will be given along with support information to take away. All participants will be using a continuous glucose monitoring system to record their blood glucose levels and will have a ketone meter to record ketone levels as advised. At each visit glucose and ketone readings will be reviewed with the participant and further advice on diabetes management given as required.

**Genital/Urinary Tract Infections:** Advice will be given on the risk of urogenital infection given at the randomisation visit as per standard initiation of SGLT2 inhibitors.

**Volume Depletion:** Advice will be given regarding "sick day rules" as per the STOP-DKA protocol

**Deterioration in renal function:** renal function will be assessed at visits 3, 5 and 7.

**Attendance at research visits:** where possible visits can be carried out via telephone or video calls.

**Monitoring of glucose and ketone levels:** PPI review highlighted that this may be a burden for participants. This has been kept to a minimum whilst still ensuring participant safety. All participants will be using continuous glucose monitoring (CGM) systems as standard care for people with type 1 diabetes, glucose monitoring will not therefore be more than usual for this population. We will encourage all participants to use a mobile app which records readings from the CGM this can be shared with the research team to allow for review of glucose readings for diabetes management and reduces the need for participants to document glucose readings.

Where is the study run from?

Ninewells Hospital and Medical School (UK)

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

January 2024 to June 2026

Who is funding the study?

Juvenile Diabetes Research Foundation United Kingdom

Who is the main contact?

Dr Joel Rocha, [sophist-trial@dundee.ac.uk](mailto:sophist-trial@dundee.ac.uk)

**Study website**

<https://sites.dundee.ac.uk/sophist-trial/>

## Contact information

**Type(s)**

Scientific, Principal Investigator

**Contact name**

Dr Ify Mordi

**Contact details**

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i.mordi@dundee.ac.uk

**Type(s)**

Public

**Contact name**

Dr Joel Rocha

**Contact details**

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Tayside Medical Science Centre (TASC)  
Residency Block, Level 3 George Pirie Way  
Ninewells Hospital and Medical School  
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+44 (0)1382 388596  
sophist-trial@dundee.ac.uk

**Additional identifiers****EudraCT/CTIS number**

Nil known

**IRAS number**

1007807

**ClinicalTrials.gov number**

NCT06435156

**Secondary identifying numbers**

01-50-23, IRAS 1007807, CPMS 61046

**Study information****Scientific Title**

A phase 2 double-blind randomised controlled trial studying the effect of sotagliflozin 200mg once daily versus placebo in individuals with heart failure and type 1 diabetes on quality of life measured using the Kansas City Cardiomyopathy Questionnaire

## **Acronym**

SOPHIST

## **Study objectives**

Primary objectives:

To investigate the effect of sotagliflozin 200mg once daily in addition to standard of care on quality of life

Secondary objectives:

1. To investigate the effect of sotagliflozin 200mg once daily in addition to standard of care on walking distance
2. To investigate the effect of sotagliflozin 200mg once daily in addition to standard of care on NT-proBNP
3. To investigate the effect of sotagliflozin 200mg once daily in addition to standard of care on glycaemic control
4. To provide information on safety and tolerability of sotagliflozin 200mg once daily in addition to standard of care compared to placebo

## **Ethics approval required**

Ethics approval required

## **Ethics approval(s)**

Approved 11/03/2024, Yorkshire & The Humber - Leeds West Research Ethics Committee (NHSBT Newcastle Blood Donor Centre, Holland Drive, Newcastle upon Tyne, NE2 4NQ , United Kingdom; +44 207 104 8141; leedswest.rec@hra.nhs.uk), ref: 24/YH/0028

## **Study design**

Interventional double-blind randomized parallel group placebo-controlled trial

## **Primary study design**

Interventional

## **Secondary study design**

Randomised parallel trial

## **Study setting(s)**

Hospital

## **Study type(s)**

Safety, Efficacy

## **Participant information sheet**

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

## **Health condition(s) or problem(s) studied**

## Type 1 Diabetes, Heart Failure

### Interventions

Participants will be randomised using an Interactive Web-based Randomisation System to one of two groups: active vs placebo 1:1

Active arm: Sotagliflozin 200 mg oral tablets once per day for 16 weeks

Placebo arm: Matching placebo, 200 mg oral tablets once per day for 16 weeks

Participants in both arms will be assessed during the treatment period (i.e. 16 weeks) and at follow-up 4 weeks later (i.e. week 20).

### Intervention Type

Drug

### Pharmaceutical study type(s)

Prophylaxis, Therapy

### Phase

Phase II

### Drug/device/biological/vaccine name(s)

Sotagliflozin

### Primary outcome measure

Quality of life measured using the change from baseline in the Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score (Weeks 0 and 16)

### Secondary outcome measures

1. Quality of life measured using the change from baseline in the KCCQ clinical summary score (Weeks 0 and 4)
2. Quality of life measured using the change from baseline in the KCCQ overall summary score (Weeks 0, 4 and 16)
3. Quality of life measured using the proportion of participants with a  $\geq 5$ ,  $\geq 10$  and  $\geq 15$  point increase in KCCQ clinical and overall summary scores (Weeks 0 and 16)
4. Quality of life measured using the change from baseline in the Diabetes Treatment Satisfaction Questionnaire (Weeks 0 and 16)
5. Quality of life measured using the change from baseline in EQ-5D-5L questionnaire score (Weeks 0 and 16)
6. Walking distance measured using the change from baseline in distance covered during 6-minute walk test (Weeks 0 and 16)
7. NT-proBNP measured using the change from baseline in NT-proBNP (Week 0 and 16)
8. Glycaemic control measured using the change from baseline in HbA1c (Week 0 and 16)
9. Safety and tolerability compared to placebo measured using the proportion of participants with level 2 or level 3 hypoglycaemia (Week 0 to 16 and 20)
10. Safety and tolerability compared to placebo measured using the proportion of participants with diabetic ketoacidosis (Week 0 to 16 and 20)
11. Safety and tolerability compared to placebo measured using the proportion of participants requiring hospitalisation due to heart failure (Week 0 to 16 and 20)

### Overall study start date

18/01/2024

**Completion date**

01/06/2026

## Eligibility

### Key inclusion criteria

1. Age 18 years to <85 years.
2. Type 1 diabetes.
3. Insulin dose  $\geq 0.5$  units/kg body weight at screening or BMI  $\geq 25$  kg/m<sup>2</sup> at screening
4. Using continuous glucose monitor at screening or willing to use one for the duration of the trial.
5. Diagnosis of heart failure (HF) regardless of left ventricular ejection fraction (LVEF), defined as one or more of the following:
  - 5.1. Previous HF hospitalisation where HF was documented as the primary cause of hospitalisation and there was a requirement for loop diuretics
  - or
  - 5.2. Impaired left ventricular (LV) function (i.e. LVEF <50% by any imaging modality) at any time
  - or
  - 5.3. Preserved LV systolic function (LVEF  $\geq 50\%$ ) with left atrial enlargement (2-dimensional echocardiographic measurement of left atrial width  $\geq 3.8$  cm or left atrial length  $\geq 5.0$  cm or left atrial area  $\geq 20$  cm<sup>2</sup> or left atrial volume index  $> 29$  ml/m<sup>2</sup>) within the last 24 months.
  - or
  - 5.4. Preserved LV systolic function (LVEF  $\geq 50\%$ ) with left ventricular hypertrophy (2-dimensional echocardiographic measurement of end-diastolic interventricular septal diameter  $\geq 1.2$  cm or end-diastolic left ventricular posterior wall diameter  $\geq 1.2$  cm) within the last 24 months.
  - or
  - 5.5. Preserved LV systolic function (LVEF  $\geq 50\%$ ) with echocardiographic diastolic dysfunction (septal  $e' < 7$  cm/sec or lateral  $e' < 10$  cm/sec or average  $E/e' \geq 15$ ) within the last 24 months.
6. New York Heart Association Class II-IV at screening.
7. Elevated N-terminal pro-B-type natriuretic peptide ( $\geq 250$  ng/L for those in sinus rhythm,  $\geq 400$  ng/L if in atrial fibrillation) or B-type natriuretic peptide ( $\geq 75$  ng/L for those in sinus rhythm,  $\geq 100$  ng/L if in atrial fibrillation) within 12 months of screening.
8. Kansas City Cardiomyopathy clinical summary score <85 at screening.

### Participant type(s)

Patient

### Age group

Adult

### Lower age limit

18 Years

### Upper age limit

85 Years

### Sex

Both

### Target number of participants

## Key exclusion criteria

Current exclusion criteria as of 12/03/2024:

1. Cardiac surgery (coronary artery bypass graft or valve replacement), type 1 myocardial infarction, implantation of cardiac device (including biventricular pacemaker) or cardiac mechanical support implantation within 1 month of screening, or between screening and randomisation, or planned during the trial.
2. End-stage heart failure requiring left ventricular assist devices, intra-aortic balloon pump, or any type of mechanical support at the time of randomisation.
3. Documented primary severe valvular heart disease, amyloidosis or hypertrophic cardiomyopathy as principal cause of heart failure as judged by the local investigator.
4. Respiratory disease thought to be the primary cause of dyspnoea as assessed by the local investigator.
5. Chronic kidney disease with estimated glomerular filtration rate  $<25\text{ml/min/1.73m}^2$  at screening.
6. Moderate or severe hepatic impairment (e.g. Child-Pugh B and C) at screening as judged by the local investigator.
7. Use of sotagliflozin or any SGLT2 inhibitor within 1 month of screening or between screening and randomisation.
8. Previous hypersensitivity/intolerance to SGLT2 inhibitors.
9. Presence of malignancy with expected life expectancy  $<1$  year at screening.
10. Severe hypoglycaemia (hospitalisation for hypoglycaemia or episode requiring external assistance to treat) within 1 month prior to screening or between screening and randomisation.
11. One episode of diabetic ketoacidosis or nonketotic hyperosmolar state within 1 month of screening or between screening and randomisation, or  $\geq 2$  diabetic ketoacidosis or nonketotic hyperosmolar state events within 6 months of screening.
12. Pregnant or lactating women.
13. Women of childbearing age or male partners of women of childbearing age and not practicing an acceptable method of birth control, see section 8.11
14. On a ketogenic diet.
15. Unwilling/unable to share glucose and ketone monitoring data.
16. Unwilling to wear continuous glucose monitoring during the trial.
17. Use of any investigational drugs within five times of the elimination half-life after the last dose or within 30 days, whichever is longer. Current enrolment in non-interventional, observational studies will be allowed.

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Previous exclusion criteria:

1. Cardiac surgery (coronary artery bypass graft or valve replacement), type 1 myocardial infarction, implantation of cardiac device (including biventricular pacemaker) or cardiac mechanical support implantation within 1 month of screening, or between screening and randomisation, or planned during the trial.
2. End-stage heart failure requiring left ventricular assist devices, intra-aortic balloon pump, or any type of mechanical support at the time of randomisation.
3. Documented primary severe valvular heart disease, amyloidosis or hypertrophic cardiomyopathy as principal cause of heart failure as judged by the local investigator.
4. Respiratory disease thought to be the primary cause of dyspnoea as assessed by the local investigator.

5. Chronic kidney disease with estimated glomerular filtration rate  $<25\text{ml/min/1.73m}^2$  at screening.
6. Severe hepatic impairment at screening as judged by the local investigator.
7. Use of sotagliflozin or any SGLT2 inhibitor within 1 month of screening or between screening and randomisation.
8. Previous hypersensitivity/intolerance to SGLT2 inhibitors.
9. Presence of malignancy with expected life expectancy  $<1$  year at screening.
10. Severe hypoglycaemia (hospitalisation for hypoglycaemia or episode requiring external assistance to treat) within 1 month prior to screening or between screening and randomisation.
11. One episode of diabetic ketoacidosis or nonketotic hyperosmolar state within 1 month of screening or between screening and randomisation, or  $\geq 2$  diabetic ketoacidosis or nonketotic hyperosmolar state events within 6 months of screening.
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14. On a ketogenic diet.
15. Unwilling/unable to share glucose and ketone monitoring data.
16. Unwilling to wear continuous glucose monitoring during the trial.
17. Use of any investigational drugs within five times of the elimination half-life after the last dose or within 30 days, whichever is longer. Current enrolment in non-interventional, observational studies will be allowed.

**Date of first enrolment**

28/01/2025

**Date of final enrolment**

01/11/2025

## **Locations**

**Countries of recruitment**

England

Scotland

United Kingdom

**Study participating centre**

**Ninewells Hospital**

Ninewells Avenue

Dundee

United Kingdom

DD1 9SY

**Study participating centre**

**Leicester General Hospital**

Gwendolen Road



Leicester  
United Kingdom  
LE5 4PW

**Study participating centre**  
**Moorgreen Hospital**  
Botley Road  
West End  
Southampton  
United Kingdom  
SO30 3JB

**Study participating centre**  
**Addenbrookes**  
Addenbrookes Hospital  
Hills Road  
Cambridge  
United Kingdom  
CB2 0QQ

**Study participating centre**  
**Wythenshawe Hospital**  
Southmoor Road  
Wythenshawe  
Manchester  
United Kingdom  
M23 9LT

**Study participating centre**  
**St George's Healthcare Nhs**  
Blackshaw Road  
London  
United Kingdom  
SW17 0QT

**Study participating centre**  
**Royal Infirmary of Edinburgh**  
51 Little France Crescent  
Old Dalkeith Road

Lothian  
United Kingdom  
EH16 4SA

**Study participating centre**

**Prince Philip Hospital**

Bryngwynmawr  
Dafen  
Llanelli  
United Kingdom  
SA14 8QF

**Study participating centre**

**Glasgow Royal Infirmary**

84 Castle Street  
Glasgow  
United Kingdom  
G4 0SF

**Study participating centre**

**Manchester Royal Royal Infirmary**

Cobbett House  
Oxford Road  
Manchester  
United Kingdom  
M13 9WL

**Study participating centre**

**North Manchester Healthcare NHS Trust**

North Manchester General Hospital  
Delaunays Road  
Crumpsall  
Manchester  
United Kingdom  
M8 5RB

**Study participating centre**

**Aberdeen Royal Infirmary**

Foresterhill Road

Aberdeen  
United Kingdom  
AB25 2ZN

**Study participating centre**  
**Northern General Hospital**  
Northern General Hospital NHS Trust  
C Floor, Huntsman Building  
Herries Road  
Sheffield  
United Kingdom  
S5 7AU

**Study participating centre**  
**Guys Hospital**  
Guys Hospital  
Great Maze Pond  
London  
United Kingdom  
SE1 9RT

**Study participating centre**  
**University Hospital Aintree**  
Longmoor Lane  
Liverpool  
United Kingdom  
L9 7AL

## **Sponsor information**

**Organisation**  
University of Dundee

**Sponsor details**  
Ninewells Hospital and Medical School  
Dundee  
Scotland  
United Kingdom  
DD1 9SY  
+44 (0)1382 383297  
TASCgovernance@dundee.ac.uk

**Sponsor type**

University/education

**Website**

<https://www.dundee.ac.uk/tasc/>

**ROR**

<https://ror.org/03h2bxq36>

## **Funder(s)**

**Funder type**

Charity

**Funder Name**

Juvenile Diabetes Research Foundation United Kingdom

**Alternative Name(s)**

Juvenile Diabetes Research Foundation Ltd, JUVENILE DIABETES RESEARCH FOUNDATION LIMITED, JDRF UK, JDRF

**Funding Body Type**

Government organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

United Kingdom

## **Results and Publications**

**Publication and dissemination plan**

Peer reviewed scientific journals

Internal report

Conference presentation

Publication on website

Submission to regulatory authorities

Other

Consent will be sought for data to be shared for the purposes of research. Any information which identifies the participant will be removed prior to sharing.

**Intention to publish date**

01/06/2027

## **Individual participant data (IPD) sharing plan**

Datasets of pseudo-anonymised individual participant data generated and/or analysed during the current study will be available upon request from the Chief Investigator Dr Ify Mordi (i. mordi@dundee.ac.uk) at the end of the trial (i.e. when all endpoints/outcomes have been met, key analyses are complete and results published in peer-reviewed scientific journals). Data will remain available for at least 25 years.

Data will only be released for legitimate secondary research purposes, where the Chief Investigator (Dr Ify Mordi) agrees that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request.

Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any existing contractual obligations. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.

## **IPD sharing plan summary**

Available on request