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Sotagliflozin in patients with heart failure symptoms and type 1 diabetes

Submission date	Recruitment status	[X] Prospectively registered
23/01/2024	Recruiting	[_] Protocol
Registration date	Overall study status	[_] Statistical analysis plan
12/03/2024	Ongoing	[_] Results
Last Edited	Condition category	[_] Individual participant data
11/05/2026	Nutritional, Metabolic, Endocrine	[X] 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 October 2027

Who is funding the study?
Breakthrough T1D: Type 1 Diabetes (formerly Juvenile Diabetes Research Foundation United Kingdom).

Who is the main contact?
Ms Susan Long, sophist-trial@dundee.ac.uk

Contact information

Type(s)

Scientific, Principal investigator

Contact name
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Type(s)
Public

Contact name
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Additional identifiers

ClinicalTrials.gov (NCT)
NCT06435156

Integrated Research Application System (IRAS)
1007807

Central Portfolio Management System (CPMS)
61046

Protocol serial number
01-50-23

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

Study type(s)
Efficacy, Safety

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

Phase

Phase II

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

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

Key secondary outcome(s))
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 ≥5, ≥10 and ≥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)

Completion date
31/10/2027

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 11/05/2026:
1. Age 18 years to <85 years.
2. Type 1 diabetes.
3. Insulin dose ≥0.5 units/kg body weight at screening or BMI ≥25kg/m2 at screening
4. Using a continuous glucose monitor at screening or willing to use one for the duration of the trial.
5. Diagnosis of heart failure (HF) or high-risk for HF, defined as any of the following:
5.1. NT- pro-BNP ≥250ng/L for those in atrial fibrillation/flutter, ≥125 ng/L for those in all other rhythms
or
5.2. Previous HF hospitalisation where HF was documented as the primary cause of hospitalisation and there was a requirement for loop diuretics
or
5.3. Impaired left ventricular (LV) function (i.e. LVEF <50% by any imaging modality) at any time

or
5.4. Preserved LV systolic function (LVEF ≥50%) with left atrial enlargement (2-dimensional measurement of left atrial width ≥3.8cm or left atrial length ≥5.0 cm or left atrial area ≥20cm2 or left atrial volume index >29 ml/m2) within the last 24 months.
or
5.5. Preserved LV systolic function (LVEF ≥50%) with left ventricular hypertrophy (2-dimensional measurement of end-diastolic interventricular septal diameter ≥1.2cm or end-diastolic left ventricular posterior wall diameter ≥1.2cm) within the last 24 months.
or
5.6. Preserved LV systolic function (LVEF ≥50%) with diastolic dysfunction (septal e' <7cm/sec or lateral e' <10cm/sec or average E/e' ≥15) within the last 24 months.
6. New York Heart Association Class II-IV at screening.
7. Kansas City Cardiomyopathy clinical summary score <85 at screening.

Previous key inclusion criteria:
1. Age 18 years to <85 years.
2. Type 1 diabetes.
3. Insulin dose ≥0.5 units/kg body weight at screening or BMI ≥25kg/m2 at screening
4. Using a 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 ≥50%) with left atrial enlargement (2-dimensional echocardiographic measurement of left atrial width ≥3.8cm or left atrial length ≥5.0 cm or left atrial area ≥20cm2 or left atrial volume index >29 ml/m2) within the last 24 months.
or
5.4. Preserved LV systolic function (LVEF ≥50%) with left ventricular hypertrophy (2-dimensional echocardiographic measurement of end-diastolic interventricular septal diameter ≥1.2cm or end-diastolic left ventricular posterior wall diameter ≥1.2cm) within the last 24 months.
or
5.5. Preserved LV systolic function (LVEF ≥50%) with echocardiographic diastolic dysfunction (septal e' <7cm/sec or lateral e' <10cm/sec or average E/e' ≥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 (≥250 ng/L for those in sinus rhythm, ≥400 ng/L if in atrial fibrillation) or B-type natriuretic peptide (≥75 ng/L for those in sinus rhythm, ≥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

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 years

Upper age limit
85 years

Sex
All

Total final enrolment
0

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 <25ml/min/1.73m² 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 ≥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.

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 <25ml/min/1.73m² 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.
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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
30/04/2027

Locations

Countries of recruitment
United Kingdom

England

Scotland

Study participating centre

Ninewells Hospital
Ninewells Avenue
Dundee
Scotland
DD1 9SY

Study participating centre
Leicester General Hospital
Gwendolen Road
Leicester
England
LE5 4PW

Study participating centre
Moorgreen Hospital
Botley Road
West End
Southampton
England
SO30 3JB

Study participating centre
Addenbrookes
Addenbrookes Hospital
Hills Road
Cambridge
England
CB2 0QQ

Study participating centre
Wythenshawe Hospital
Southmoor Road
Wythenshawe
Manchester
England
M23 9LT

Study participating centre
St George's Healthcare Nhst
Blackshaw Road
London

England
SW17 0QT

Study participating centre
Royal Infirmary of Edinburgh
51 Little France Crescent
Old Dalkeith Road
Lothian
Scotland
EH16 4SA

Study participating centre
Prince Philip Hospital
Bryngwynmawr
Dafen
Llanelli
Wales
SA14 8QF

Study participating centre
Glasgow Royal Infirmary
84 Castle Street
Glasgow
Scotland
G4 0SF

Study participating centre
Manchester Royal Royal Infirmary
Cobbett House
Oxford Road
Manchester
England
M13 9WL

Study participating centre
North Manchester Healthcare NHS Trust
North Manchester General Hospital
Delaunays Road
Crumpsall

Manchester
England
M8 5RB

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
Scotland
AB25 2ZN

Study participating centre
Northern General Hospital
Northern General Hospital NHS Trust
C Floor, Huntsmnan Building
Herries Road
Sheffield
England
S5 7AU

Study participating centre
Guys Hospital
Guys Hospital
Great Maze Pond
London
England
SE1 9RT

Study participating centre
University Hospital Aintree
Longmoor Lane
Liverpool
England
L9 7AL

Study participating centre
Sherwood Forest Hospitals NHS Foundation Trust
Kings Mill Hospital
Mansfield Road

Sutton-in-ashfield
England
NG17 4JL

Study participating centre
University Hospitals Sussex NHS Foundation Trust
Worthing Hospital
Lyndhurst Road
Worthing
England
BN11 2DH

Sponsor information

Organisation
University of Dundee

ROR
https://ror.org/03h2bxq36

Funder(s)

Funder type
Charity

Funder Name
Breakthrough T1D: Type 1 Diabetes (formerly 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

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Study website	Study website	11/11/2025	11/11/2025	No	Yes