Introduction

SOtagliflozin in **P**atients with **H**eart fa**i**lure **S**ymptoms and **T**ype 1 Diabetes **(SOPHIST)**

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.

SOPHIST website https://sites.dundee.ac.uk/sophist-trial/

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Sponsor: University of Dundee & NHS Tayside

Background

- Heart failure (HF) related morbidity and mortality is an increasing problem in type 1 diabetes.
- Sotagliflozin has been shown to improve quality of life and heart failure related outcomes in patients with type 2 diabetes, chronic kidney disease and heart failure symptoms.
- No trials have examined the effect of sotagliflozin in individuals with type 1 diabetes and heart failure symptoms.

Purpose of trial

- To investigate the effect of 16-week treatment with sotagliflozin in addition to standard of care on quality of life compared to placebo in participants with type 1 diabetes and HF symptoms.

Target sample size

- 320 participants with type 1 diabetes and heart failure symptoms

Treatment allocation

- Participants will be randomised in a 1:1 allocation ratio to:

Arms	Dosage and form	Frequency
Sotagliflozin	200 mg oral tablet	Once daily for 16 weeks
Matched placebo	200 mg oral tablet	

Sotagliflozin

- Is a dual Sodium-glucose co-transporter (SGLT)1 and 2 inhibitor.

- Initially developed as an oral add-on treatment for glycaemic control in type 2 diabetes but large cardiovascular outcome trials have reported a significant ~30% risk reduction in hospitalisation for HF, as well as overall reductions in cardiovascular mortality.

- Currently does not have marketing authorisation in the UK but is in the National Institute for Health and Care Excellence (NICE) published guidance as an option for individuals with type 1 diabetes with:
  - Body mass index (BMI) ≥27kg/m^2
  - Insulin need of at least 0.5 units/kg of body weight
  - Inadequate glycaemic control despite optimal insulin therapy.

- Approved in May 2023 for use in the United States of America by the Food and Drug Administration in all patients with HF without limitations on use in individuals with type 1 diabetes.

Primary objective

- To investigate the effect of 16-week treatment with sotagliflozin (200mg once daily) in addition to standard of care on quality of life compared to placebo in participants with type 1 diabetes and HF symptoms.

Outcome Measure:

- Change in Kansas City Cardiomyopathy Questionnaire (KCCQ) clinical summary score from baseline to 16 weeks.

Secondary objectives

- To investigate the effect of sotagliflozin (200mg once daily) in addition to standard of care on:
  - Quality of life (KCCQ, Diabetes Treatment Satisfaction Questionnaire and EQ-5D-5L)
  - Walking distance (6-minute walk test)
  - NT-proBNP
  - Glycaemic control (HbA1c)

- To provide information on safety and tolerability of sotagliflozin 200mg once daily in addition to standard of care compared to placebo (proportion of level 2 and 3 hypoglycaemic events, diabetic ketoacidosis and hospitalisations due to heart failure).

Exploratory objectives

- To investigate the effect of sotagliflozin (200mg once daily) in addition to standard of care on:
  - Heart failure symptoms, signs and clinical outcomes (NYHA, daily loop diuretic dose, blood pressure and number of hospitalisations/deaths due to heart failure)
  - Renal parameters (eGFR, serum creatinine and urine albumin to creatinine ratio)
  - Diabetes-related parameters (Insulin dose, body weight)
  - Continuous glucose monitor metrics (Mean glucose level, Percentage time above, below and in range and glycaemic variability index)
  - Ketone levels (proportion of non-acidotic ketosis events)

- To investigate if trial outcomes are associated with baseline c-peptide levels.