An Exploratory, Randomized, Double-blind, Placebo-controlled, Parallel Arm Trial of the Safety and Pharmacodynamic Activity of Sotagliflozin in Hemodynamically Stable Patients with Worsening Heart Failure

Published: 24-10-2017
Last updated: 12-04-2024

The main objective of this study is to test the effects of combined SGLT1 and SGLT2 inhibition with sotagliflozin on hemoconcentration and plasma volume in patients with heart failure.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON46513

Source
ToetsingOnline

Brief title
PDY15079

Condition

- Heart failures

Synonym
Acute Heart Failure, worsening of Heart Failure

Research involving
Human

Sponsors and support

Primary sponsor: Sanofi-aventis
Source(s) of monetary or material Support: Sanofi

Intervention

Keyword: Acute Heart failure, worsening heart failure

Outcome measures

Primary outcome

- Assess the safety and tolerability of sotagliflozin in hemodynamically stable patients with worsening of heart failure

- Estimate the effects of sotagliflozin on plasma volume changes in hemodynamically stable patients with worsening of heart failure

Secondary outcome

- Explore the effect of sotagliflozin on erythropoiesis, as assessed by changes in plasma erythropoietin levels, in hemodynamically stable patients with worsening of heart failure, compared to placebo

- Explore the effect of sotagliflozin on changes in plasma NT-proBNP levels, in hemodynamically stable patients with worsening of heart failure, compared to placebo

Study description

Background summary

Sotagliflozin (SAR439954) is a dual inhibitor of sodium-glucose co-transporter 1 and 2 (SGLT1 and SGLT2). The compound, a member of the pharmaceutical class of SGLT-inhibitors known as gliflozins, lowers blood glucose by decreasing and delaying SGLT1-mediated glucose absorption in the gastrointestinal tract as well as enhancing glucose excretion in the urine by reducing renal glucose

re-absorption via action of SGLT2 in the kidney.

The outcome of the EMPA-REG trial showed improvement in CV mortality and was not a result of reduced MI or stroke, but rather was mediated by a reduction in heart failure hospitalization and death. As non-diabetic patients with heart failure patients may also have favorable volume changes and may also benefit from SGLT inhibition, and thus both diabetic and non-diabetic heart failure patients will be enrolled in the PDY15079 trial.

Study objective

The main objective of this study is to test the effects of combined SGLT1 and SGLT2 inhibition with sotagliflozin on hemoconcentration and plasma volume in patients with heart failure.

Study design

Phase 2, randomized, double blind study with parallel groups.

Intervention

Sotaglifozin 200 mg, 400 mg of placebo for 14 days

Study burden and risks

Risks and burdens related to blood collection, study procedures and possible adverse events of the investigational medicinal product.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

-18 years of age or older.;-Patient admitted to the hospital or had urgent visit to emergency department or heart failure unit/clinic for Congestive Heart Failure, defined by:;-Presence of *2 of the following clinical signs and symptoms of congestion: jugular venous distension, pitting edema in lower extremities greater than trace, dyspnea, rales heard on auscultation, radiographic pulmonary congestion, weight gain above historical dry weight of at least 5 lbs (2.27 kg) and requiring treatment with IV diuretics (*2 bolus doses or continuous infusion).;-Estimated glomerular filtration rate (eGFR) *30 mL/min/1.73m^2 at the screening or randomization visit by the 4 variable Modification of Diet in Renal Disease (MDRD) equation.
-Transitioning from IV to oral diuretics and oral diuretic treatment has been prescribed or administered.
-Hemodynamically stable, defined as:
-SBP *100 mmHg with no requirement for IV inotropic therapy or IV vasodilators

Exclusion criteria

-History of Type 1 diabetes mellitus.;-Current admission or visit for Worsening HF that is clearly and primarily triggered by causes such as tachyarrhythmia (example: sustained ventricular tachycardia, or atrial fibrillation/flutter with sustained ventricular response > 130 beats per minute), acute coronary syndrome, pulmonary embolism, cerebrovascular accident, heart valve disorders (such as severe aortic stenosis), as determined by the Investigator.;- Clinically significant myocardial infarction (MI) within past 1 month as determined by Investigator and with objective evidence from ECG, and/or cardiac imaging and/or coronary angiography. Small isolated elevations in troponin that often accompany HF hospitalization are not an exclusion, nor are clinically significant MIs that have been revascularized without complications ;- patients who recently had or sceduled to have cardiac interventions may be eligible if:
-stable 48 hours post procedure and

-have diuretic treatment planned for the duration of treatment planned for the duration of treatment in this study.;- Current use of or recent suspension of digoxin therapy with high levels of digoxin (level should be obtained and must be <1.2 ng/mL) at screening.;-History of heart or kidney transplant.;- Diagnosis of hypertrophic obstructive cardiomyopathy.;- End-stage HF defined as requiring left ventricular assist device insertion, intra-aortic balloon placement (IABP), or any type of mechanical support during the study period.;- Use of any investigational drug(s) or prohibited therapy or sodium-glucose co-transporter 2 (SGLT2) inhibitor 5 half-lives prior to screening.;- Patients with moderate or severe respiratory, moderate and severe hepatic, neurological, psychiatric, active malignant tumor or other major systemic disease (including any diseases with evidence of malabsorption), making implementation of the protocol and/or the interpretation of the study results difficult.;- Known allergies, hypersensitivity, or intolerance to sotagliflozin or any inactive component of sotagliflozin or placebo (ie, microcrystalline cellulose, croscarmellose sodium [disintegrant], talc, silicon dioxide, and magnesium stearate [non-bovine]), unless the reaction is deemed irrelevant to the study by the PI.;- Laboratory findings at the Screening Visit:;-Alanine aminotransferase (ALT) or aspartate aminotransferase (AST) >3 times the upper limit of the normal laboratory range (ULN) (1 repeat lab allowed);;-Total bilirubin >1.7 times the ULN (except in case of Gilbert*s syndrome) (1 repeat lab allowed);;-Amylase and/or lipase > 3 times the ULN (1 repeat lab allowed);- Patients with a severe or persistent in spite of optimal treatment genitourinary tract infection at time of randomization.;- Patient is the Investigator or any Sub investigator, research assistant, pharmacist, study coordinator, other staff or relative thereof directly involved in the conduct of the protocol.;- History of diabetic ketoacidosis or non-ketotic hyperosmolar coma within 3 months prior to the screening visit.;- Lower extremity diabetic complication (such as skin ulcers, infection, osteomyelitis and gangrene) identified during the Screening period, and still requiring treatment at Randomization.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	13-09-2018
Enrollment:	6
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	NVT
Generic name:	sotagliflozin

Ethics review

Approved WMO Date:	24-10-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-01-2018
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-06-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	31-08-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-12-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	18-02-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-04-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-06-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2017-002774-39-NL
ClinicalTrials.gov	NCT03292653
CCMO	NL63463.042.17