A Randomized, Double-blind, Placebo-controlled, Parallel-group, Multicenter Study to Evaluate the Effects of Sotagliflozin on Clinical Outcomes in Hemodynamically Stable Patients with Type 2 Diabetes post Worsening Heart Failure

Published: 19-03-2018
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON50219

Source
ToetsingOnline

Brief title
SOLOIST-WHF

Condition

- Heart failures
- Diabetic complications

Synonym

Diabetes Mellitus type 2

Research involving
Human

Sponsors and support

Primary sponsor: Lexicon Pharmaceuticals, Inc.
Source(s) of monetary or material Support: Lexicon Pharmaceuticals;Inc.

Intervention

Keyword: Cardiovascular events, Diabetes Type 2, Heart failure, Sotagliflozin

Outcome measures

Primary outcome

The primary objectives of this study are:

-To demonstrate that sotagliflozin reduces cardiovascular (CV) mortality and morbidity (composite of CV death or hospitalization for heart failure [HHF]) compared to placebo in hemodynamically stable patients with type 2 diabetes (T2D) and heart failure (HF) with a left ventricular ejection fraction (LVEF) <50%, after admission for worsening heart failure (WHF).

-To demonstrate that sotagliflozin reduces CV mortality and morbidity (composite of CV death or HHF) compared to placebo in hemodynamically stable patients with T2D and heart failure, irrespective of LVEF.

Secondary outcome

The secondary objectives of this study are:

-To demonstrate that, when compared to placebo, in the total patient population, sotagliflozin reduces the total number (ie, including recurrent events) of the following clinical events:

-Cardiovascular death, HHF, or urgent HF visit

-To demonstrate that, when compared to placebo, sotagliflozin reduces:

-The composite of positively adjudicated sustained *50% decrease in estimated glomerular filtration rate (eGFR) from Baseline (for *30 days), chronic dialysis, renal transplant or positively adjudicated sustained eGFR <15 mL/min/1.73 m2 (for *30 days) in the total patient population

-Cardiovascular death in patients with LVEF <50%

-Cardiovascular death in the total patient population

-All-cause mortality in patients with LVEF <50%

-All-cause mortality in the total patient population

-To demonstrate the safety and tolerability of sotagliflozin in the total patient population.

Study description

Background summary

Heart failure (HF) is the most common cause of hospitalization of patients over the age of 65.
Type 2 diabetes is a growing epidemic worldwide that is associated with a high incidence of
macrovascular and microvascular complications. The Emerging Risk Factors Collaboration has recently reported that patients with T2D have a doubled risk of CV death compared to patients without diabetes. Cardiovascular complications of diabetes include myocardial infarction (MI), stroke, and HF.

Sotagliflozin (SAR439954) is a dual inhibitor of sodium-glucose co-transporter 1 and 2 (SGLT2 and SGLT1).

Recent data indicate that SGLT2 inhibitors may reduce HF morbidity and mortality in patients with T2D. These antihyperglycemic agents lower blood glucose levels, in part, through the inhibition of renal glucose reabsorption thereby enhancing renal glucose excretion.

Increased renal glucose excretion and therefore osmotic diuresis, one of the main hypotheses of the mechanism of action on HF, has been seen in patients with T2D who have received sotagliflozin.

Study objective

The main objectives of the study are to demonstrate whether sotagliflozin reduces the composite of CV (cardiovascular) death and HHF (hospitalization for heart failure) as compared to placebo in diabetic patients after admission for WHF (worsening heart failure).

Study design

This study is a Phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group study in about 4000 hemodynamically stable patients with T2D who have been admitted to the hospital, a HF unit, infusion center, or Emergency Department (ED) for WHF with intravascular volume overload. The study will consist of 3 periods:
* A Screening period (up to 14 days)
* A Randomized, double-blind treatment period that will include an initial up-titration period
* A Post-treatment period of 14 days

Intervention

Randomized patients will receive sotagliflozin 200 mg or placebo 1 tablet during the first 2 weeks. At week 3 and beyond sotagliflozin randomized patients will receive 400 mg and placebo randomized patients will receive 2 tablets.

Study burden and risks

Risk and burdens related to blood collections, study procedures and possible adverse events of study medication.

Contacts

Public
Lexicon Pharmaceuticals, Inc.

Technology Forest Place 8800
The Woodlands TX 77381-1160
US
Scientific
Lexicon Pharmaceuticals, Inc.

Technology Forest Place 8800
The Woodlands TX 77381-1160
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- patients diagnosed with T2D
- Patient admitted to the hospital or had unplanned HF visit to ED, Heart Failure Unit, or
infusion center for WHF associated with intravascular volume overload (the Index Event),
as determined by Investigator AND received treatment with IV diuretics
- Patient had a diagnosis of HF *3 months prior to Screening
- Prior chronic treatment (or prescription) with a loop diuretic (eg, furosemide, torsemide,
bumetanide) for *30 days prior to the Index Event
- Patients with LVEF <40% should be on beta-blockers and RAAS inhibitors as per local
guidelines unless contraindicated
- Patient is hemodynamically stable,
- Transitioning from IV to oral diuretics

Exclusion criteria

-Age <18 years (or legal age for the country of participation) or >85 years at the Screening Visit
-Index Event (admission for worsening HF associated with intravascular volume overload * see I 02) primarily triggered by pulmonary embolism, cerebrovascular accident, or acute myocardial infarction (AMI)
-Index Event (admission for WHF * see I 02) for WHF not caused primarily by intravascular volume overload.
-Hospitalization for index event >2 weeks
-Acute coronary syndromes within 3 months prior to Randomization
-Ejection fraction not assessed at time of Randomization
-End-stage HF
-Cardiac surgery (coronary artery bypass graft), percutaneous coronary intervention (PCI), implantation of cardiac device (including biventricular pacemaker), or cardiac mechanical support implantation within 1 month prior to Randomization or planned during the study
-Hemodynamically significant uncorrected primary cardiac valvular disease
-Significant pulmonary disease contributing substantially to the patients* dyspnea such as forced expiratory volume in 1 second, or any kind of primary right heart failure such as primary pulmonary hypertension or recurrent pulmonary embolism
-Heart failure caused by postpartum cardiomyopathy diagnosed within the past 6 months
-Heart failure from uncorrected thyroid disease, active myocarditis, known amyloid cardiomyopathy, or hypertrophic obstructive cardiomyopathy
-Obstructive hypertrophic cardiomyopathy
-History of stroke within 3 months prior to Randomization
-History of dialysis within 1 year prior to Randomization
-History of solid organ transplant or inclusion on a transplant list (if a heart transplant, defined as status 1 transplant)
-Use of any investigational drug(s) for 5 half-lives prior to Screening
-Hypersensitivity to sotagliflozin active substance or to any of the excipients
-Patients who are planning to start a sodium-glucose cotransporter 2 (SGLT2) inhibitor (other than study drug) during the study.
-Any SGLT2 inhibitor <1 month prior to the Screening Visit, or between Screening and Randomization
-Patients with respiratory, hepatic, neurological, psychiatric, or active malignant tumor (except for non-melanoma skin cancers, which are not exclusionary) or other major systemic disease (including any diseases with evidence of malabsorption or severe anemia) or patients with short life expectancy
-Severe kidney disease at the Screening or Randomization
-Any infection requiring intravenous antibiotics and/or with pyrexia (defined as temperature >38 °C [100.4 °F]) at time of Randomization
-History of diabetic ketoacidosis or nonketotic hyperosmolar coma within 3

months prior to the Screening Visit
-Lower extremity diabetic complications (such as skin ulcers, infection, osteomyelitis and gangrene) identified during the Screening period, and still requiring treatment at Randomization
-Pregnant (demonstrated by serum pregnancy test at Screening) or breastfeeding women
-Women of childbearing potential not willing to use a highly-effective method(s) of birth control during the study treatment period and the Follow-up period, or who are unwilling or unable to be tested for pregnancy

Study design

Design

Study phase:	3
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):	22-11-2018
Enrollment:	65
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	19-03-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	04-07-2018
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-08-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	07-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-01-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-02-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	05-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	02-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	23-12-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-03-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-04-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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
Other	2017-003510-16
EudraCT	EUCTR2017-003510-16-NL
CCMO	NL64869.100.18