AstraZeneca

ZENITH - D4325C00010

elixia

Title:

A Phase III, Randomised, Multicentre, Double-blind Study to Evaluate the Efficacy, Safety, and Tolerability of Zibotentan/Dapagliflozin Compared to Dapagliflozin Alone in Participants with Chronic Kidney Disease and High Proteinuria (ZENITH High Proteinuria)

Overview

The purpose of the study is to evaluate the efficacy, safety, and tolerability of zibotentan and dapagliflozin in FDC (fixed-dose combination) versus dapagliflozin alone, on top of current SoC, in participants with CKD and high proteinuria. Urinary albumin to creatinine ratio is an established key surrogate marker. High, or high residual UACR and UPCR are predictors of more rapid progression of kidney disease

Indication:

Patient with CKD and high proteinuria, with or without type 2 diabetes mellitus (T2DM)

Objectives & Endpoints

Objectives (Primary): To determine whether zibotentan and dapagliflozin in FDC is superior to dapagliflozin alone to slow decline in kidney function.

Endpoints(Primary): Change in eGFR from baseline to Month 24.

Study Compensation:

$100 per visit ($50 for phone visit) up to a total of $1450.

Study Duration:

The study consists of 3 periods: a screening period with run-in, a double-blind treatment period for up to 2 and a follow-up period not more than 28 days

Investigational Product:

Approximately 1500 participants who meet eligibility criteria will be randomized to one of 2 treatment arms in a 1:1 ratio:

- Zibotentan/dapagliflozin 10 mg FDC QD
- Dapagliflozin 10 mg QD (active comparator)

Major Eligibility Criteria:

Major Inclusion Criteria:	**Major Exclusion Criteria:**

• CKD with
  ➢ eGFR ≥ 20 and < 90 mL/min/1.73m &
  ➢ UACR > 700 mg/g (> 79 mg/mmol) or UPCR > 1000 mg/g (> 113 mg/mmoL).
• Receiving RAASi therapy (ACEi or ARB), and for the patient maximum tolerated labelled daily dose, that has been stable for at least 4 weeks
	• CHD class III or class IV
	• Hospitalized for HF during the last 6 months, heart disease or COVID-19 during the last 6 months
	• Type 1 diabetes mellitus
	• Systolic blood pressure above 160 mmHg or below 90 mmHg.
	• History of solid organ transplantation
	• Malignancy within the past 5 years.
	• Renal replacement therapy or previous kidney transplant
	• Drug or alcohol abuse
	• Participants on strong or moderate CYP3A4 inducer, systemic immunosuppression therapy