Lilly

J3L-MC-EZEF
ACCLAIM-Lp(a)

elixia

Title:

A Phase 3, Randomized, Double-Blind, Placebo-Controlled Study to Investigate the Effect of Lepodisiran on the Reduction of Major Adverse Cardiovascular Events in Adults with Elevated Lipoprotein(a) who have Established Atherosclerotic Cardiovascular Disease or Are at Risk for a First Cardiovascular Event – ACCLAIM-Lp(a)

Overview

- Approximately 12,500 participants will be randomly assigned in a 1:1 ratio to receive either lepodisiran or placebo, added to their existing standard-of-care background medications.
- The first 3 doses are 6 months apart. All remaining doses are 12 months apart (Q12M) until the end of the study..

This is an event-driven study, the median study duration will be approximately 4 years until at least 1276 participants experience at least 1 component event of the primary composite endpoint.

Indication:

Subjects with established ASCVD or at risk for first CV event

Objectives & Endpoints

The primary objectives of Study is to demonstrate whether lepodisiran is superior to placebo in reducing the risk of the composite endpoint of MACE-4, defined as

CV death	Nonfatal Myocardial Infarction	Nonfatal Stroke	Urgent Coronary Revascularization

Study Compensation:

Varied from $56 to $84 per visit (Visit 1: $112) up to a total of $1900.

Study Duration:

As this is an event-driven study, the median study duration will be approximately 4 years until at least 1276 participants experience at least 1 component event of the primary composite endpoint. The minimum study duration for each participant is expected to be 2 years.

The study consists of 1, Optional Prescreening Visit, 2, Screening Period up to 6-week
3, Treatment Period minimum of 2 year, 4, Final Visit 30 days.

Investigational Product:

Lepodisiran sodium (lepodisiran) is a novel Dicer-substrate siRNA oligonucleotide designed to reduce the levels of LPA mRNA and Apo(a) expression and thereby to decrease the Lp(a) level. Lepodisiran is being developed to reduce the risk of MACE in patients with high levels of Lp(a) and established ASCVD or at risk of CV events.

Major Eligibility Criteria:

Major Inclusion Criteria: (Check Protocol for detail)

- Lp(a) ≥175 nmol/L
- Have the disease characteristics of either 2a **OR** 2b:
  - **2a:** Established ASCVD with history of an event or revascularization >90 days
  - **2b:** Risk for a first CV event with **ONE** of the following:
    - CAD or PAD
      OR
    - Known Familial Hypercholesterolemia
      OR
    - Participants must have **3 or more** of these risk factors: Elderly (≥65 for men, ≥ 70 for women), CKD, HTN, DM, CAC, Hyperlipidemia, Current tobacco use, hsCRP>2 mg/L (9.05 nmol/L), Family history of premature ASCVD

Major Exclusion Criteria:

- Have had a major CV event or surgery < 90 days
- Uncontrolled Hypertension
- New York Heart Association class IV Heart Failure
- Known Coronary Artery Calcium Score of 0.
- Lipoprotein Apheresis
- Severe Renal Failure - eGFR <15 mL/min/1.73
- Active Nephrotic Syndrome, or UACR of ≥5000 mg/g
- Acute or Chronic Hepatitis
- Malignant Neoplasms within the past 5 years
- Active Infection Or Major Disease that is not currently stable
- Substance Use
- Taken lepodisiran, muvalaplin, pelacarsen, olpasiran, zerlasiran, obicetrapib, or any medication used or under investigation for lowering Lp(a).