DepleTTR-CM Study Overview

Protocol Number: ALXN2220-ATTRCM-301

A phase 3, randomized, double-blind, placebo-controlled, multicenter study to evaluate the safety and effectiveness of amyloid depleter ALXN2220 in adult participants with transthyretin amyloid cardiomyopathy (ATTR-CM).

Study Purpose

The purpose of the DepleTTR-CM Study is to evaluate the safety and effectiveness of an amyloid depleter investigational medication in adults 18 to 90 years of age as compared to placebo in treating adults with ATTR-CM. This is a depleter study, which aims to target the active removal of pre-existing amyloids and restore heart function and elasticity.

Study Participation

The DepleTTR-CM Study is enrolling approximately 1,000 adult participants across approximately 28 countries. Participants may still be able to remain on standard-of-care therapies.

Eligible participants must:

- Be 18 to 90 years of age
- Have a confirmed diagnosis of ATTR-CM with transthyretin (TTR) that is either
  - wild-type TTR
    OR
  - a variant TTR genotype
- Be willing to be genetically tested for mutations in the *TTR* gene
- NOT have received prior treatment with an ATTR amyloid depleter

About the DepleTTR-CM Study

Participants will be assigned at random to receive either the investigational medication or a placebo. Neither the participant nor the study team will know which treatment option has been assigned, but in case of an emergency, the study team can quickly find out. Both the investigational medication and the placebo are administered every four weeks as a one- to two-hour intravenous (IV) infusion, meaning fluid will be administered through a vein.

Parts of the Study

Participation in the DepleTTR-CM Study may last up to about two and a half to four and a half years. Potential participants will have a 35-day screening period in which the study team will perform tests and procedures to see if they are eligible to participate.

If they are eligible and decide to join the study, they will enter the treatment period, which lasts two to four years and includes 56 study site visits. Following an infusion, participants will be observed for two hours by the study team. Some visits require blood samples to be collected two hours before receiving the assigned study treatment.

After a participant's last dose of their assigned study treatment, they will visit the study site twice, once every two months over a four-month period, to complete final tests and assessments to evaluate their health. Participants who complete the treatment period may be eligible to enroll in the open-label extension (OLE) study. During the OLE study, all participants will receive the investigational medication, even if they received the placebo in the DepleTTR-CM Study.

The Goal of This Study

The primary goal of this study is to evaluate the safety and effectiveness of the investigational medication, ALXN2220, compared to a placebo. To determine if amyloid deposits are being removed, body imaging assessments as well as blood sample collections may be performed. Participants will also undergo reviews of their health changes during visits, which include questionnaires regarding their heart symptoms and quality of life. The effectiveness will also be measured by a six-minute walk test, during which participants will walk at a normal pace for six minutes to evaluate how their body systems are working while exercising.

Thank you for your interest in the DepleTTR-CM Study. For more details on eligibility or to learn more information, please visit DepleTTRCMStudy.com.

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