Study to Check the Safety of Fazirsiran and Learn if Fazirsiran Can Help People With Liver Disease and Scarring (Fibrosis) Due to an Abnormal Version of Alpha-1 Antitrypsin Protein

Status: RECRUITING

Eligibility Criteria

Age: 18 years to 75 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion criteria: * The participant must have a diagnosis of the Z allele homozygotes (PiZZ) genotype AATD. PiZZ diagnosis from source verifiable medical records is permitted. Otherwise, participants must undergo PiZZ confirmatory testing (genotyping for PiS and PiZ alleles) at screening. PiMZ or PiSZ genotypes are not permitted. * The participant, of any sex, is aged 18 to 75 years, inclusive. * The participant's liver biopsy core sample collected should meet the requirements of the protocol. * The participant has evidence of METAVIR stage F2, F3, or F4 liver fibrosis, evaluated by a centrally read baseline liver biopsy during the screening period; or confirmed as meeting all the entry criteria by central reading of a previous biopsy conducted within 6 months before the estimated enrollment date using an adequate liver biopsy and slides as defined in the study laboratory manual. * The participant has a pulmonary status meeting the protocol's requirements. * It must be confirmed that the participant does not have HCC. Participants will be screened for HCC with alpha-fetoprotein (AFP) and abdominal ultrasound. If the participant has any of the following, they will be required to have contrast-enhanced CT or MRI imaging to exclude HCC before randomization. * An adult participant must have a body mass index (BMI) between 18.0 and 39.0 kilograms per meter square (kg\^m2), inclusive. * The participant is a nonsmoker for at least 6 months before screening. Exclusion Criteria * The participant has a history of liver decompensating events (overt hepatic encephalopathy \[West Haven Grade \>=2\] documented by a physician, clinically significant ascites, spontaneous bacterial peritonitis, GI bleeding from varices, hepatopulmonary syndrome, hepatorenal syndrome, portal pulmonary hypertension, or bleeding portal hypertensive gastropathy). * The participant has a history of the presence of medium or large varices or varices with red wale signs based on a previous esophagogastroduodenoscopy (EGD) within 6 months before the estimated enrollment date. For certain participants, an EGD will be required at screening if there is no EGD available within 6 months before the estimated enrollment date. Presence of small varices with no red wale signs on EGD and no history of bleeding will be acceptable for study eligibility. * The participant has evidence of other forms of chronic liver diseases, including viral hepatitis B or C, primary biliary cholangitis, primary sclerosing cholangitis, Wilson disease, alcoholic hepatitis, hemochromatosis, liver cancer, history of biliary diversion, or autoimmune hepatitis. * The participant has alanine transaminase (ALT) or aspartate transaminase (AST) levels \>250 units per liter (U/L). * The participant has a platelet count \<60,000 per cubic millimeter (mm\^3) (\<60 × 10\^9 per liter \[10\^9/L\]). * The participant has albumin \<=2.8 gram per deciliter (g/dL) (28 grams per deciliter \[g/L\]). * The participant has international normalized ratio (INR) \>=1.7. * The participant is expected to have severe and unavoidable high-level exposure to inhaled pulmonary toxins during the study such as may occur with occupational exposure to mineral dusts or metals. * The participant has a history of drug abuse (such as cocaine, phencyclidine) within 1 year before the screening visit or has a positive urine drug screen at screening. * The participant has previously been treated with fazirsiran or any other RNAi for AATD-LD. * The participant has portal vein thrombosis. * The participant has a prior transjugular portosystemic shunt procedure. * The participant has a history of malignancy within the last 5 years, except for adequately treated basal cell carcinoma, squamous cell skin cancer, superficial bladder tumors, or in situ cervical cancer. Participants with other curatively treated malignancies who have no evidence of metastatic disease and a greater than 1-year disease-free interval may be entered after approval by the medical monitor.

Conditions & Interventions

Interventions:

DRUG: Fazirsiran Injection, OTHER: Placebo

Conditions:

Alpha1-Antitrypsin Deficiency

More Information

Contact(s): Takeda Contact - medinfoUS@takeda.com

Principal Investigator:

Phase: PHASE3

IRB

Number:

System ID: NCT05677971
