Liver Cirrhosis Network Rosuvastatin Efficacy and Safety for Cirrhosis in the United States

Status: RECRUITING

Eligibility Criteria

Age: 18 years to 75 years old

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Age 18-75 years 2. Cirrhosis due to nonalcoholic steatohepatitis, alcohol-associated liver disease, or chronic viral hepatitis (treated hepatitis B virus or hepatitis C virus) 3. Clinical diagnosis of cirrhosis as defined investigator confirmation and the following: 1. At least one liver biopsy within 5 years prior to consent showing either: Metavir stage 4 fibrosis; Ishak Stage 5-6 fibrosis, OR 2. At least 2 of the following: i. Evidence on imaging: Nodular liver with either splenomegaly or recanalized umbilical vein within the past 48 weeks ii. Liver stiffness: vibration-controlled transient elastography within 48 weeks prior to consent or during Screening ≥15 kilopascal or magnetic resonance elastography within 48 weeks prior to consent or during Screening ≥5 kilopascal iii. Evidence of varices demonstrated on imaging or endoscopy within 3 years prior to consent or during Screening iv. Either: Fibrosis-4\>2.67 or platelets \<150/mL within 6 months prior to consent or during Screening 4. Two measures of vibration-controlled transient elastography: one at screening and one at the randomization study visit, meeting the following criteria: 1. The first measure must be ≥ 15 kilopascal. 2. The two measures must be at least 2 hours apart and no more than 60 days apart from one another. 3. The mean of two measurements must be ≥ 15 kilopascal. 4. Additionally, both screening and open-label dispense liver stiffness measures must be ≤50 kPa 5. Compensated defined by: 1. Absence of ascites/hydrothorax, hepatic encephalopathy or variceal bleeding currently or in the last 48 weeks, as determined clinically by investigator. 2. If prior history of decompensation, must be without current symptoms of decompensation and no longer requiring treatment of complications for the last 48 weeks, including the use of diuretics for the treatment of ascites, and/or rifaximin or lactulose for the treatment of hepatic encephalopathy. Use of non-selective beta blockers will be allowed. 3. Child-Pugh score \<8 6. Provision of written informed consent.

Exclusion Criteria:

1. Currently on a statin or any statin exposure within 24 weeks prior to consent. 2. Known indication for statin therapy, defined as: 1. Prior peripheral vascular, cardiovascular or cerebrovascular event for which statins are indicated for secondary prevention, OR 2. Documented familial hypercholesterolemia, heterozygous familial hypercholesterolemia, OR 3. Fasting LDL-C ≥ 190 mg/dL 3. Myocardial infarction, Unstable angina, transient ischemic events, or stroke within 24 weeks of screening. 4. Alcohol Use Disorder Identification Test (AUDIT) total score of ≥8 at screening. 5. Patients with limitations in attending study visits. 6. Prisoners. 7. Known prior or current hepatocellular carcinoma (HCC) or cholangiocarcinoma. 8. Known transjugular intrahepatic portosystemic shunt (TIPS), balloon retrograde transvenous obliteration (BRTO) or porto-systemic shunt surgery regardless of time of occurrence. 9. Current (in past 24 weeks prior to consenting) use of medications known to cause hepatic fibrogenesis or confound endpoint assessment, defined as: 1. amiodarone 2. methotrexate 3. warfarin 10. Current (in past 24 weeks prior to consenting) use of medications which may increase risk for rosuvastatin-related myositis or DILI, defined as: 1. fenofibrate 2. erythromycin 3. gemfibrozil 4. niacin (500 mg or more) 5. HIV protease inhibitors (darunivar, indinavir, nelfinavir, amprenavir) in patients of East Asian descent 6. colchicine 7. cyclosporin 8. Additional medications that will be excluded: atazanavir/ritonavir capmatinib darolutamide dasabuvir/ombitasvir/paritaprevir/ritonavir ledipasvir/sofosbuvir elbasvir/grazoprevir erythromycin glecaprevir/pibrentasvir lopinavir/ritonavir regorafenib ritonavir, in any combination simeprevir sofbuvir/velpatasvir/voxilaprevir sofosbuvir/velpatasvir tafamidis teriflunomide *If exposure was for 7 or less days for one of these medications can consider enrollment after 28 days from final dose. 11. Presence of portal or hepatic vein thrombosis 12. Diagnosis of untreated hypothyroidism or on unstable treatment regimen for hypothyroidism 13. Receiving an elemental diet or parenteral nutrition 14. Chronic pancreatitis or pancreatic insufficiency 15. Etiology of cirrhosis other than ALD, NAFLD, or viral hepatitis (excluded diagnoses include cryptogenic immune-mediated such as AIH, PSC and PBC, cardiac cirrhosis or Fontan-associated liver disease, A1AT, Wilson's disease, etc.) 16. Conditions which may confound study outcome: 1. Unstable or active inflammatory bowel disease 2. Active infection 3. Any malignant disease (other than squamous or basal cell carcinoma of the skin) within previous 3 years 4. Prior solid organ or hematopoietic cell transplant 5. Bariatric surgery in the last 24 weeks prior to consent or planned bariatric surgery within the next 96 weeks 6. Current liver-unrelated end-stage organ failures such as end-stage renal disease on dialysis, stage 3-4 congestive heart failure (CHF), current chronic obstructive pulmonary disease (COPD) on home oxygen. 17. Known current medical or psychiatric conditions which, in the opinion of the investigator, would make the participant unsuitable for the study for safety reasons or interfere with or prevent adherence to the protocol. 18. The following laboratory abnormalities within 90 days of screening: 1. Hemoglobin \<10 g/dL 2. Albumin \<3.0 g/dL 3. Prolonged international normalized ratio (INR) \>1.5 4. Total bilirubin ≥ 2.0 mg/dl (unless due to Gilbert's syndrome or hemolysis as denoted by normal direct bilirubin fraction) 5. Direct bilirubin ≥ 0.9 6. Uncontrolled diabetes (HbA1c ≥ 9.5%) within past 90 days. 19. Kidney function abnormalities including: 1. Dialysis 2. Baseline eGFR \< 30 cc/min with CKD-Epi equation 3. Known nephrotic proteinuria, defined as 3g or greater of protein in 24-hour urine collection 20. Recent (within 48 weeks) or present hepatic decompensation with ascites/hydrothorax, hepatic encephalopathy or variceal bleeding 21. Untreated chronic hepatitis B or C infection 1. HCV eligible for enrollment if HCV RNA negative at baseline or documentation of prior SVR12 2. HBV eligible if an HBV DNA \<100 IU/mL within the last 48 weeks and on treatment 22. Serum aspartate aminotransferase (AST) or alanine aminotransferase (ALT) ≥ 200 U/L, or alkaline phosphatase (ALP) ≥ 300 within the past 24 weeks. 23. Documented history of intolerance to statins 24. Serious comorbid medical disease which in the investigator's opinion renders a life-expectancy less than 96 weeks 25. Active illicit substance use (other than THC), including inhaled or injected drugs, in the 24 weeks prior to screening 26. Pregnancy, planned pregnancy or breastfeeding 27. Current participation in active medication treatment trials (within 24 weeks prior to randomization) or planned participation in active medication treatment trials simultaneous to participation in present trial. 28. Significant existing muscle pain or tenderness or prior history of myasthenia gravis as determined by a site physician. 29. Failure or inability to provide informed consent.

Conditions & Interventions

Interventions:

DRUG: Rosuvastatin

Conditions:

Cirrhosis, Cirrhosis, Liver, Cirrhosis Early, Cirrhosis Due to Hepatitis B, Cirrhosis Advanced, Cirrhosis Infectious, Cirrhosis Alcoholic, Cirrhosis Due to Hepatitis C

Keywords:

Cirrhosis, Liver, Nonalcoholic Fatty Liver Disease

More Information

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Principal Investigator:

Phase: PHASE2

IRB

Number:

System ID: NCT05832229

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