

ASSURE 1

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Sponsor:

C5 Research – Cleveland Clinic Coordinating Center for Clinical Research

Study Purpose:

ApoA1 Synthesis Stimulation in Acute Coronary Syndrome Patients
Phase II multi-center, double-blind, randomized, parallel group, placebo-controlled clinical trial for the assessment of lipid and coronary plaque changes with RVX000222 in patients with acute coronary syndrome events

Objective:

The primary objective of this study is to determine the early effects of RVX000222 on the change in ApoA1 in patients with a recent ACS event who require coronary angiography

Inclusion Criteria:

1. Male and female patient's ≥ 18 years of age who are scheduled to undergo coronary angiography for a clinically indicated reason.
2. Women of child-bearing potential, that is, women not surgically sterilized and between menarche and 1 year post menopause, must test negative for pregnancy at the time of enrollment based on a serum pregnancy test and agree to use a reliable method of birth control (for example, use of oral contraceptives or Norplant®; a reliable barrier method of birth control (diaphragms with contraceptive jelly; cervical caps with contraceptive jelly; condoms with contraceptive foam; intrauterine devices; partner with vasectomy; or abstinence) during the study and for one month following the last dose of study drug.
3. Patients within 4 weeks of an acute coronary syndrome.
4. Patients must meet all of the following criteria at the qualifying coronary catheterization procedure:

Entire Coronary Circulation:

Angiographic evidence of coronary heart disease as defined by at least one lesion in any of the three major native coronary arteries that has $> 20\%$ reduction in lumen diameter by angiographic visual estimation or prior history of PTCA. This vessel need not be the target coronary artery for IVUS. Any vessel with previous PTCA may not be used as the target coronary artery.

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Left Main Coronary Artery:

Must not have a > 50% reduction in lumen diameter by visual angiographic estimation.

Target Coronary Artery for IVUS

Must be accessible to the IVUS catheter. Must have a < 50% reduction in lumen diameter by angiographic visual estimation throughout a segment of at least 40 mm in length (the "target segment"). A lesion of up to 60% stenosis is permitted, distal to the target segment. A single branch of the "target vessel" may have a narrowing up to but <70% by visual estimation, as long as the target segment contains no lesion >50%, provided that the branch in question is not a target for PCI or CABG. Has not undergone prior percutaneous coronary intervention or coronary artery bypass graft surgery. The target vessel is not currently a candidate for intervention or a likely candidate for intervention over the next 6 months. The target vessel may not be a bypass graft. The target vessel may not be a bypassed vessel. The target vessel may not be the culprit vessel for a previous MI.

5. Patients that do not meet IVUS criteria following the coronary angiogram can be evaluated for non-IVUS inclusion.
6. Have given signed informed consent to participate in this study.

Exclusion Criteria:

1. Clinically significant heart disease which will require coronary bypass, PCI, cardiac transplantation, surgical repair and/or replacement during the course of the study.
2. Coronary artery bypass graft (CABG) procedure within the past 90 days.
3. Previous or current diagnosis of severe heart failure (NYHA Class III/IV) or a documented left ventricular ejection fraction (LVEF) of < 25% as determined by contrast left ventriculography, radionuclide ventriculography or echocardiography. The absence of an LVEF measurement in a patient without a previous or current diagnosis of heart failure does not prohibit entry into the study.
4. Patients with evidence of cardiac electrophysiologic instability including a history of uncontrolled ventricular arrhythmias, uncontrolled atrial fibrillation/flutter or uncontrolled supraventricular tachycardias with a ventricular response heart rate of > 100 beats per minute at rest within 4 weeks prior to Visit 1.
5. Evidence of renal impairment as determined by any one of the following: serum creatinine > 1.5 mg/dL, a history of dialysis, or a history of nephrotic syndrome.
6. Have hypertension that is uncontrolled defined as 2 consecutive measurements of sitting blood pressure of systolic >160 mm Hg or diastolic > 95 mm Hg at Visit 1.

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7. Pregnant or nursing (lactating) women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive β -hCG laboratory test (≥ 5 mIU/mL).

8. Current or recent (within 12 month prior to Visit 1) treatment with immunosuppressants (eg, Cyclosporine).

9. No use of fibrates or niacin 90 days prior to Visit 1.

10. Triglycerides > 400 mg/dL at Visit 1.

11. Any medical or surgical condition which might significantly alter the absorption, distribution, metabolism or excretion of medication including, but not limited to any of the following: cholecystitis, Crohn's disease, ulcerative colitis, or any gastric bypass alteration.

12. Evidence of hepatic disease as determined by any one of the following:

- ALT, AST values exceeding $1.5 \times$ ULN at Visit 1
- a history of hepatic encephalopathy
- a history of esophageal varices
- or a history of portocaval shunt.

13. A total bilirubin that is $>$ ULN at Visit 1.

14. History of malignancy of any organ system, treated or untreated, within the past 5 years whether or not there is evidence of local recurrence or metastases, with the exception of localized basal cell carcinoma of the skin.

15. History or evidence of drug or alcohol abuse within the last 12 months.

16. Any surgical or medical condition, which in the opinion of the investigator, may place the patient at higher risk from his/her participation in the study, or is likely to prevent the patient from complying with the requirements of the study or completing the study.

17. Use of other investigational drugs and devices at the time of enrollment, or within 30 days or 5 half-lives of enrollment, whichever is longer.

18. History of noncompliance to medical regimens or unwillingness to comply with the study protocol.

19. Any condition that in the opinion of the investigator would confound the evaluation and interpretation of efficacy and/or safety data.

20. Persons directly involved in the execution of this protocol.

Status:

Active enrollment

If you have any questions, please feel free to contact the coordinators, and they will be happy to answer any questions you have regarding this study.