

DAL PLAQUE II

Principal Investigator:

William Felten, MD (Mid-Michigan)

Sub-Investigators:

Rodney Diehl, MD

Sponsor:

F. HOFFMANN-LA ROCHE LTD

Study Purpose:

Protocol NC22703: A Phase IIIB multicenter, double-blind, randomized, placebo-controlled study, evaluating the effect of treatment with dalcetrapib 600 mg on Atherosclerotic Disease as measured by I. Coronary Intravascular Ultrasound (IVUS) and Quantitative Coronary Angiography II Carotid B-Mode Ultrasound Intima Media Thickness (IMT) and total plaque volume in subjects undergoing coronary angiography who have coronary artery disease (CAD)

Objective:

To evaluate the effect of dalcetrapib treatment for 2 years on atherosclerotic disease progression - as assessed by coronary intravascular ultrasound (IVUS) and carotid B-mode ultrasound - in patients with coronary artery disease (CAD)

Inclusion Criteria:

1. Male and female patients over the age of 18 years.
2. Patients scheduled for clinically indicated coronary angiography and possible ad hoc percutaneous coronary intervention (PCI) will be evaluated before their scheduled procedure.
3. Written informed consent (approved by the Institutional Review Board [IRB]/Independent Ethics Committee [IEC]) obtained prior to any study specific screening procedures.
4. Patients considered to be stable at screening (at the discretion of the investigator) are eligible provided they meet all other entry criteria.
5. Evidence-based management of LDL-C cholesterol, at a minimum to include medical and dietary treatment to a target level of <100 mg/dl (<2.6 mmol/L) by the time of randomization, and ideally to include treatment to a target level <70 mg/dl (<1.8 mmol/L). Patients with an LDL-C level above ≥ 100 mg/dL (≥ 2.6 mmol/L) may be randomized if they cannot reach the target goal of less than 100 mg/dL despite an intensive statin regimen, are on a maximum tolerated dose of statin as determined by the investigator, or are unable to tolerate statins.

Imaging inclusion criteria:

6. A MAX IMT ≥ 0.65 mm, as measured off-line and documented in the core ultrasound lab, in either one (or both) of the common carotid arterial far walls, and an overall visualization of $\geq 4/6$ analyzable arterial right and left carotid arterial segments.

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7. Angiographic inclusion criteria:

- Entire Coronary Circulation: The patient must have angiographic evidence of coronary artery 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 PCI. This vessel does not need to be the target coronary artery for IVUS. Any vessel with previous PCI may not be used as the target coronary artery.
- Left Main Coronary Artery: The patient must not have >50% reduction in lumen diameter by visual angiographic estimation.
- Target Coronary Artery: Patients will be required to have one "target" coronary artery for IVUS that has not undergone prior PCI, that is not a candidate to undergo present PCI or in the next 24 months, and that has not been the cause of a recent myocardial infarction. The proximal 4 cm of the "target" artery in which IVUS examination will be performed at baseline:
 - must have a diameter stenosis < 50% in lumen diameter by visual assessment of the angiogram;
 - must have a reference diameter > 2.5 mm;
 - must be free of filling defects suggestive of thrombus;
 - must not present any anatomical characteristic (such as but not limited to severe tortuosity or calcification) that would impede IVUS interrogation at baseline or follow-up. A lesion of up to 60% stenosis is permitted, distal to the target segment. A side branch of the target coronary artery for IVUS may not be a target for PCI.

Exclusion Criteria:

Patients will **NOT** be entered/randomized into the study if they satisfy any of the following criteria:

1. Women of childbearing potential (women who are not surgically sterile or postmenopausal defined as amenorrhea for >12 months) who are not using a highly effective contraceptive method (failure rate less than 1% per year) such as implants, injectibles, combined oral contraceptives or hormonal intrauterine devices (IUDs). In addition, a negative urine or serum pregnancy test must be available before randomization for all women of childbearing potential.

2. Baseline IVUS study determined to be of unacceptable quality by the IVUS core laboratory due to but not limited to the following conditions:

- the presence of excessive calcium observed during the IVUS pullback sequence, precluding measurement of cross-sectional area if more than 90 degrees of circumference is involved;
- non-uniform rotational distortion of the IVUS transducer, resulting in image artifacts;
- submission of an IVUS interrogation of a target coronary artery segment which is too short;
- poor IVUS image quality due to inadequate saline flushing of the IVUS catheter.

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3. MAX IMT > 3.0 mm and/or a clinically symptomatic and/or relevant arterial stenosis as assessed by ultrasound Doppler, in any of the carotid arterial segments.
4. Previous coronary artery bypass graft (CABG) surgery or probable need for CABG in the next 24 months.
5. Myocardial infarction in the target coronary artery for IVUS between the initial IVUS examination and randomization.
6. Patients who have symptomatic congestive heart failure (CHF) (New York Heart Association [NYHA] Class III or IV) at baseline.
7. Patients with clinically significant valvular heart disease likely to require surgical repair or replacement during the treatment period of the study.
8. Patients previously hypersensitive to a CETP inhibitor, have received a CETP vaccine, or have previously participated in any clinical trial using dalcetrapib or another CETP inhibitor.
9. Any clinically significant medical condition or presence of any laboratory abnormality performed prior to randomization that is considered by the investigator to be clinically important and could interfere with the conduct of the study.
10. Uncontrolled blood pressure: Systolic blood pressure ≥ 180 mmHg and/or diastolic blood pressure ≥ 110 mmHg at screening or any other pre-randomization visit despite antihypertensive therapy.
11. Concomitant treatment with any drug other than dalcetrapib administered for the purpose of increasing levels of HDL-C (niacin, fibrates). Treatment with ezetimibe or fish oil derivatives is permitted.
12. History of obstructive biliary disorders, pancreatitis, collagen diseases, active liver disease, or auto-immune diseases.
13. Aspartate aminotransferase (AST [SGOT]), alanine aminotransferase (ALT [SGPT]) or bilirubin levels ≥ 1.5 x ULN at screening.
14. Unexplained creatine phosphokinase levels > 3 times the ULN at screening.
15. Poorly controlled diabetes mellitus (HbA1c > 10%) as measured at screening.
16. eGFR < 30 mL/min at screening.
17. Triglycerides level > 400 mg/dL (4.52 mmol/L) at screening.
18. Patients with a life expectancy less than 2 years.
19. History of malignancy (except for curatively treated basal cell or squamous cell carcinoma of the skin) during the 3 years prior to the screening.
20. Patients with homozygous or heterozygous familial hypercholesterolemia.
21. Females who are pregnant or breast-feeding.
22. History of alcohol or drug abuse within 3 years prior to screening or current drug or alcohol abuse.
23. Patients who have received an investigational drug or device within 30 days of screening visit, or who expect to participate in any other investigational drug or device study during the conduct of this trial.

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24. Unable or unwilling to comply with protocol requirements, or deemed by the investigator to be unfit for the study.

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.