

REVEAL

NCT01252953

Principal Investigator: Dr. John Collins, MD (St. Mary's of Michigan)

Condition: Atherosclerotic Cardiovascular Disease

Drug: anacetrapib vs. placebo

Official Title: REVEAL: Randomized EVAluation of the Effects of Anacetrapib Through Lipid-modification (REVEAL)

Sponsor: University of Oxford

Purpose: The Randomized EVAluation of the Effects of Anacetrapib Through Lipid-modification (REVEAL) trial aims to determine whether lipid modification with anacetrapib 100mg daily reduces the risk of coronary death, myocardial infarction (MI) or coronary revascularization (collectively known as major coronary events) in patients with circulatory problems who have their Low-density Lipoprotein (LDL) cholesterol level treated with a statin.

Inclusion Criteria:

- Patients must be aged at least 50 at the time of initial invitation, and at least one of the following inclusion criteria must be satisfied:
 - History of MI; or
 - Cerebrovascular atherosclerotic disease (i.e. history of presumed ischaemic stroke or carotid revascularization); or
 - Peripheral arterial disease (i.e. history of non-coronary revascularization, including aortic aneurysm repair or graft); or
 - Diabetes mellitus with other evidence of symptomatic coronary heart disease (i.e. treatment or hospitalization for angina, or a history of coronary revascularization or acute coronary syndrome).

Exclusion Criteria:

- None of the following must be satisfied:
 - Acute MI, acute coronary syndrome or stroke within 4 weeks prior to Screening Visit or during Run-in (but such individuals may be entered later, if appropriate);
 - Planned coronary revascularization procedure within the next 6 months (such individuals may be entered later, if appropriate);
 - Definite history of chronic liver disease, or abnormal liver function (i.e. alanine transaminase (ALT) >2x the upper limit of normal (ULN)). Note: Individuals with a history of acute hepatitis are eligible provided this ALT limit is not exceeded;
 - Severe renal insufficiency (i.e. creatinine >200 µmol/L [2.3 mg/dL], dialysis or functioning renal transplant);
 - Evidence of active inflammatory muscle disease (e.g. dermatomyositis, polymyositis), or creatine kinase (CK) >3x ULN;
 - Previous significant adverse reaction to a statin or anacetrapib;
 - Current treatment with any of the following lipid-lowering treatments:
 - a regimen considered to produce substantially greater LDL cholesterol reduction than atorvastatin 80 mg daily for individuals in non-Asian countries or 20 mg daily for those in North East Asia; or (ii) fibric acid derivative ("fibrate", including gemfibrozil); or (iii) niacin (nicotinic acid) at doses above 100 mg daily

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Exclusion Criteria (Continued):

- Concurrent treatment with a medication that is contraindicated with anacetrapib or atorvastatin:
 - i. any potent CYP3A4 inhibitor, such as:
 1. macrolide antibiotics (erythromycin, clarithromycin, telithromycin);
 2. systemic imidazole or triazole antifungals (e.g. itraconazole, posaconazole);
 3. protease inhibitors (e.g. atazanavir);
 4. nefazodone
 - ii. ciclosporin
 - iii. daptomycin
 - iv. systemic use of fusidic acid
- Note: Individuals who are taking such drugs temporarily may be re-screened when they discontinue them, if considered appropriate;
- Known to be poorly compliant with clinic visits or prescribed medication;
 - Medical history that might limit the individual's ability to take trial treatments for the duration of the study (e.g. severe respiratory disease; history of cancer or evidence of spread within last 5 years, other than non-melanoma skin cancer; or recent history of alcohol or substance misuse);
 - Women of child-bearing potential (unless using adequate contraception);
 - Current participation in a clinical trial with an unlicensed drug or device.

Individuals will also be excluded at the Screening visit if it is considered unlikely that they will achieve total cholesterol <3.5 mmol/L (135 mg/dL) on the highest atorvastatin dose available in their region (atorvastatin 80 mg daily in non-Asian countries or 20 mg daily in North East Asia).

In addition, individuals will be excluded at the Randomization visit if any of the following are true:

- Total cholesterol above 4 mmol/L [155 mg/dL]
- Non-compliant with run-in treatment (<90% scheduled run-in medication taken)
- Individual is no longer willing to be randomized into the 4-5 year trial
- The individual's doctor is of the view that their patient should not be randomized.

Source: <https://clinicaltrials.gov/ct2/show/NCT01252953>

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