



Andreas Vesalius
1514-1564

- Flemish anatomist and physician who was a Professor at University of Padua, known as the founder of modern anatomy who renewed the practice of human dissection
- Authored *De humani corporis fabrica (On the Fabric of the Human Body)*, which revolutionized the study of anatomy by revealing the most accurate account of human anatomy published during his time
- Studies of the vascular and circulatory systems were amongst his greatest scientific contributions, dispelling previous theories by Galen
- Accurately depicted the anatomy of the human heart, and deduced that the heart acted as a pump to move blood around the body



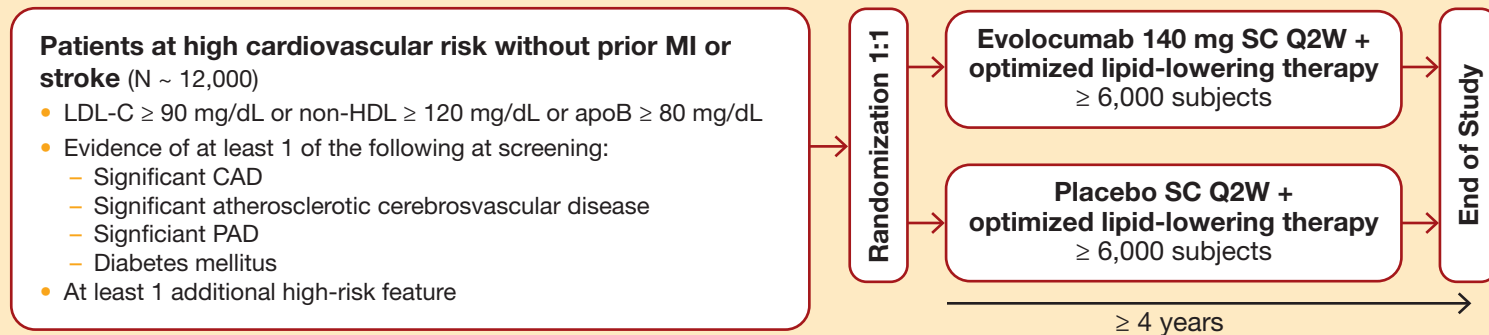
Vesalius-cv

Effect of EVolocumab in Patients at High Cardiovascular Risk Without Prior Myocardial Infarction or Stroke

Amgen Clinical Study: 20170625 NCT Clinical Study: 03872401

A Double-blind, Randomized, Placebo-controlled, Multicenter Study to Evaluate the Impact of Evolocumab on Major Cardiovascular Events in Patients at High Cardiovascular Risk Without Prior Myocardial Infarction or Stroke

PHASE 3 STUDY DESIGN*



STUDY PURPOSE:

Assess the effect of lowering LDL-C with evolocumab on major cardiovascular events in subjects without a prior MI or stroke who are at high risk for a first cardiovascular event

PRIMARY ENDPOINTS† (Time to):

- CHD death, MI, or ischemic stroke, whichever occurs first
- CHD death, MI, ischemic stroke, or any ischemia-driven arterial revascularization, whichever occurs first

SECONDARY ENDPOINTS† (Time to):

- MI, ischemic stroke, or any ischemia-driven arterial revascularization
- CHD death, MI, or any ischemia-driven arterial revascularization
- CV death, MI, or stroke
- MI
- Any ischemia-driven arterial revascularization
- CHD death
- CV death
- All-cause death
- Ischemic stroke

KEY INCLUSION CRITERIA: (All 4 needed)

- Adult subjects \geq 50 (men) or \geq 55 (women) to $<$ 80 years of age (either sex and meeting lipid criteria)
- LDL-C \geq 90 mg/dL (\geq 2.3 mmol/L) or non-HDL-C \geq 120 mg/dL (\geq 3.1 mmol/L) or apoB \geq 80 mg/dL (\geq 1.56 μ mol/L)
- Evidence of at least one of the following at screening:
 - Significant CAD
 - Significant atherosclerotic cerebrovascular disease
 - Significant PAD
 - Diabetes mellitus
- At least 1 high-risk feature

KEY EXCLUSION CRITERIA:

- MI or stroke prior to randomization
- CABG $<$ 3 months prior to screening
- Estimated glomerular filtration rate (eGFR) $<$ 15 mL/min/1.73 m²
- Fasting triglycerides \geq 500 mg/dL (5.7 mmol/L)
- Last measured left ventricular ejection fraction $<$ 30% or NYHA Functional Class III/IV

ADDITIONAL INFORMATION:

www.amgentrials.com (Protocol Number: 20170625) www.clinicaltrials.gov (Identifier: NCT03872401)

*May not be inclusive of all study details. †For adults at high cardiovascular risk without past MI or stroke and receiving optimized lipid-lowering therapy.

apoB = apolipoprotein B; CABG = coronary artery bypass graft; CAD = coronary artery disease; CHD = coronary heart disease; CV = cardiovascular; HDL-C = high-density lipoprotein cholesterol; LDL-C = low-density lipoprotein cholesterol; MI = myocardial infarction; NYHA = New York Heart Association; PAD = peripheral arterial disease; Q2W = every 2 weeks; SC = subcutaneous.