Abstract

Relationship between lipoprotein subfraction cholesterol and residual risk for cardiovascular outcomes: A post hoc analysis of the AIM-HIGH trial.

Toth PP, Jones SR, Slee A, Fleg J, Marcovina SM, Lacy M, McBride R, Boden WE.

CGH Medical Center, Sterling, IL, USA; Ciccarone Center for the Prevention of Heart Disease, Johns Hopkins University School of Medicine, Baltimore, MD, USA; Axio Research, Seattle, WA, USA; National Heart, Lung, and Blood Institute, Bethesda, MD, USA; Department of Medicine, University of Washington, Seattle, WA, USA; VA New England Healthcare System, and Massachusetts Veterans Epidemiology, Research, and Informatics Center (MAVERIC), Boston University School of Medicine, Boston, MA, USA.

BACKGROUND: The AIM-HIGH (Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglycerides and Impact on Global Health Outcomes) trial failed to demonstrate incremental clinical benefit of extended-release niacin (ERN) in 3414 statin-treated patients with established cardiovascular (CV) disease who had low baseline levels of high-density lipoprotein cholesterol (HDL-C) as compared to placebo. A previous secondary analysis suggested that ERN provided outcome benefits in ERN-treated patients with high triglycerides (TGs; >200 mg/dL) and very low HDL-C (<32 mg/dL) at baseline. The current analysis sought to ascertain how changes in TG-enriched lipoproteins and HDL subfractions impact residual risk in the comparator treatment arms.

OBJECTIVES: We evaluated the relationship between niacin treatment, lipoproteins and their subfractions, and CV outcomes in a non-prespecified, post hoc analysis of the AIM-HIGH trial.

METHODS: Lipoprotein subfraction analysis was performed with zonal ultracentrifugation in 2457 AIM-HIGH participants at baseline and 1 year of treatment. Hazard ratios were estimated using Cox proportional hazards models for relationships between lipoproteins and the composite primary endpoint of CV death, myocardial infarction, acute coronary syndrome, ischemic stroke, or symptom-driven revascularization. Analyses were performed for the entire cohort and in participants with TGs > 200 mg/dL and HDL-C < 32 mg/dL.

RESULTS: Apoprotein B-containing lipoproteins and their subfractions decreased significantly in both treatment arms but decreased more with ERN treatment. HDL-C and its subfractions increased significantly in both treatment groups, but more so in patients treated with ERN. For the entire study population, neither apoB- nor apoA1-containing lipoprotein subfractions predicted risk at baseline or at 1 year of follow-up. In the high TG and low HDL-C subgroup treated with placebo, changes at 1 year in HDL_2-C, total cholesterol/HDL_2-C, and non-HDL-C/HDL_2-C may be associated with increased CV events, whereas in the ERN treatment arm, changes at 1 year in very low-density lipoprotein cholesterol and very low-density lipoprotein subfractions, total remnant lipoproteins, and various risk ratios may be associated with increased CV events, while HDL_2-C may be associated with reduced risk.

CONCLUSIONS: We provide hypothesis-generating findings that ERN may confer benefit in patients with coronary heart disease who have high TGs and low HDL by reducing serum levels of remnant lipoprotein cholesterol and increasing HDL_2-C.

PMID: 29627296