

MYOCARDIAL ISCHEMIA AND INFARCTION

EFFECTS OF VARESPLADIB METHYL ON BIOMARKERS AND MAJOR CARDIOVASCULAR EVENTS IN ACUTE CORONARY SYNDROME PATIENTS

ACC Poster Contributions
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Background: Secretory phospholipase A2 (sPLA2) is a family of pro-atherogenic enzymes involved in lipoprotein remodeling and activation of inflammatory pathways. In acute coronary syndrome (ACS), high sPLA2-IIA levels predict major cardiovascular events (MACE).

Methods: Randomized, double-blind, prospective controlled clinical trial (Phase 2B) designed to investigate effects of sPLA2 inhibition with varespladib 500 mg (A-002) daily versus placebo as adjunctive therapy to atorvastatin 80 mg daily on LDL cholesterol (LDL-C), C-reactive protein (CRP), sPLA2 and MACE (unstable angina [UA], myocardial infarction [MI], stroke, revascularization, death) and safety. 625 ACS subjects were randomized within 96 h of index event, and treated for 16 weeks to investigate changes in biomarkers and 24 weeks to evaluate changes in clinical events and safety.

Results: Compared to placebo, varespladib reduced levels of LDL-C by 6% ($p < 0.02$) at the time of the primary endpoint and at 16 weeks, hs-CRP by 26% ($p < 0.01$) and sPLA2-IIA by 70% ($p < 0.001$) (Figure). Favorable trends were noted for UA/MI; however total MACE events were not different (varespladib 23 and placebo 24). Elevated serum transaminases were observed in 3 varespladib-treated subjects (1.0%) and 2 placebo-treated subjects (0.6%).

Conclusions: Varespladib reduced LDL-C and inflammatory biomarkers in ACS patients treated with conventional therapy including atorvastatin 80 mg daily. Based on these data, a 6500 subject Phase III trial is planned.

