A114.E1063
JACC March 9, 2010
Volume 55, issue 10A

MYOCARDIAL ISCHEMIA AND INFARCTION

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

ACC Poster Contributions
Georgia World Congress Center, Hall B5
Monday, March 15, 2010, 9:30 a.m.-10:30 a.m.

Session Title: New Insights in Treatment of Acute Coronary Syndromes
Abstract Category: Unstable Ischemic Syndrome--Clinical
Presentation Number: 1155-274

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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.