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Among patients with recent ACS, use of enzyme inhibitor does not reduce risk of cardiovascular event

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Stephen J. Nicholls, M.B.B.S., Ph.D., of the South Australian Health and Medical Research Institute and University of Adelaide, Adelaide, Australia, and colleagues determined the effects of varespladib, a drug that inhibits the enzyme secretory phospholipase A2 on cardiovascular risk in patients with acute coronary syndrome (ACS; such as heart attack or unstable angina).

Despite contemporary therapies, patients with ACS face a substantial risk of early, recurrent adverse cardiovascular events. Increasing evidence supports a potential role of inflammation in the progression and clinical instability of coronary heart disease. Secretory phospholipase A2 (sPLA2) is an enzyme involved with inflammation and implicated in atherosclerosis. The results of some studies have stimulated interest in sPLA2 inhibition as a cardioprotective strategy. The sPLA2 inhibitor varespladib has favorable effects on lipid and inflammatory markers; however, its effect on cardiovascular outcomes is unknown, according to background information in the article.

The trial was conducted at 362 academic and community hospitals in Europe, Australia, New Zealand, India, and North America and included 5,145 patients randomized within 96 hours of presentation of an ACS to either 500-mg/d varespladib (n = 2,572) or placebo (n = 2,573) for 16 weeks (study termination on March 9, 2012). The participants also received atorvastatin and other established therapies. The primary

efficacy measure was a composite of cardiovascular mortality, nonfatal heart attack, nonfatal stroke, and unstable angina with evidence of ischemia requiring hospitalization at 16 weeks. Six-month survival status was also evaluated.

At a prespecified interim analysis, including 212 patients with primary end point events, the independent data and safety monitoring board recommended termination of the trial for futility and possible harm. The primary end point occurred in 136 patients (6.1 percent) treated with varespladib compared with 109 patients (5.1 percent) treated with placebo. Varespladib was associated with a greater risk of heart attack (78 [3.4 percent] vs. 47 [2.2 percent]). The composite secondary end point of cardiovascular mortality, heart attack, and stroke was observed in 107 patients (4.6 percent) in the varespladib group and 79 patients (3.8 percent) in the placebo group.

"The sPLA2 inhibition with varespladib may be harmful and is not a useful strategy to reduce adverse cardiovascular outcomes after ACS," the authors write.

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