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ACUTE CORONARY SYNDROMES

Risk of major coronary events not reduced by darapladib therapy

Lipoprotein-associated phospholipase A_2 (Lp-PLA_2) is an enzyme found in high concentrations in unstable and ruptured atherosclerotic plates. The potential therapeutic value of blocking this enzyme was explored in the SOLID-TIMI 52 trial, designed to evaluate the efficacy and safety of darapladib (a selective inhibitor of Lp-PLA_2) in patients who had experienced an acute coronary syndrome event.

The 13,026 trial participants (patients with an acute coronary syndrome event within the previous 30 days) were randomly allocated to receive darapladib (160 mg once daily) or placebo, in addition to background guideline-recommended therapy, and were followed up for a median of 2.5 years. The primary end point (major coronary events) was a composite of myocardial infarction, urgent coronary revascularization for myocardial ischaemia, and death from coronary heart disease.

In this study, darapladib showed no effect on the risk of recurrent major coronary events. The rate of the primary end point was 16.3% in the darapladib group and 15.6% in the placebo group at 3 years (HR 1.00, 95% CI 0.91–1.09, $P = 0.93$), and rates of the individual components of the end point were also not reduced with darapladib therapy.

The results observed in the SOLID-TIMI 52 trial are at odds with reports from the STABILITY trial, in which darapladib reduced the risk of major coronary events. These discrepancies are likely to reflect the redundant nature of most inflammatory pathways, rendering highly specific inhibitors ineffective.

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Original article O'Donoghue, M. L. *et al.* Effect of darapladib on major coronary events after an acute coronary syndrome: the SOLID-TIMI 52 randomized clinical trial. *JAMA* doi:10.1001/jama.2014.11061