Anti-inflammatory drug does not reduce risk of major CV events following heart attack

April 4 2016

Michelle L. O'Donoghue, M.D., M.P.H., of Brigham and Women's Hospital, Boston, and colleagues evaluated the efficacy and safety of the anti-inflammatory drug losmapimod on cardiovascular outcomes in patients hospitalized after a heart attack. The study was published online by *JAMA*, and is being released to coincide with its presentation at the American College of Cardiology's 65th Annual Scientific Session & Expo.

Inflammation stimulated by the enzyme p38 mitogen-activated protein kinase (MAPK) is implicated in atherogenesis (the process of forming atheromas, plaques in the inner lining of arteries) and plaque destabilization. Pilot data in a phase 2 trial in patients with non-ST elevation myocardial infarction (NSTEMI; a certain pattern on an electrocardiogram following a heart attack) indicated that the p38 MAPK inhibitor losmapimod lessens inflammation and may improve outcomes. In this phase 3 trial, Dr. O'Donoghue and colleagues randomly assigned patients who had been hospitalized with an acute MI and had at least 1 additional predictor of cardiovascular risk to either twice-daily losmapimod (n = 1,738) or matching placebo (n = 1,765) on a background of guideline-recommended therapy. Patients were treated for 12 weeks and followed up for an additional 12 weeks. The study was conducted at 322 sites in 34 countries. Part A of the trial consisted of a group (n = 3,503) to provide an initial assessment of safety and exploratory efficacy before considering progression to part B (approximately 22,000 patients).

Among the 3,503 patients in part A, the primary end point (a composite of cardiovascular death, MI, or severe recurrent ischemia requiring urgent coronary revascularization with the principal analysis specified at week 12) occurred by 12 weeks in 123 patients treated with placebo (7 percent) and 139 patients treated with losmapimod (8.1 percent). The on-treatment rates of serious adverse events were 16 percent with losmapimod and 14.2 percent with placebo.

The authors write that the results of this exploratory efficacy study did not justify proceeding to a larger efficacy trial in the existing patient population.

"In this trial, losmapimod did not reduce the risk of recurrent major adverse cardiovascular events through 12 weeks of treatment in patients hospitalized with acute MI. Furthermore, there was no evidence that losmapimod reduced the incidence of any secondary outcomes including all-cause mortality. Therefore, our findings do not support a strategy of p38 MAPK inhibition with losmapimod in patients hospitalized with MI."

"Because inflammation is believed to play a key role in atherogenesis, there remains intense interest to identify an anti-inflammatory therapeutic that will reduce the risk of cardiovascular events. However, because inflammation acts along multiple redundant and interconnected pathways, the identification of an appropriate target may be difficult, and it is challenging to predict clinical efficacy prior to phase 3 testing."

More information: *JAMA*, DOI: 10.1001/jama.2016.3609

Provided by The JAMA Network Journals

Citation: Anti-inflammatory drug does not reduce risk of major CV events following heart attack (2016, April 4) retrieved 5 May 2024 from https://medicalxpress.com/news/2016-04-anti-inflammatory-drug-major-cv-events.html

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.