

Higher risks without cardio benefits halt study of aleglitazar

March 31 2014

The phase III AleCardio trial was ended early when patients with type 2 diabetes and recent acute coronary syndrome who were treated with aleglitazar showed higher rates of heart failure, kidney events and gastrointestinal bleeding with no offsetting cardiovascular benefits, according to data presented at the American College of Cardiology's 63rd Annual Scientific Session. All other studies with the drug have been stopped as well.

Aleglitazar sparked interest for this patient population because of its dual action on two subtypes of the PPAR cellular receptors. PPAR gamma helps regulate glucose; PPAR alpha does the same for lipids – fats and fat-like compounds in the blood that include cholesterol and triglycerides. Patients with [type 2 diabetes](#) were enrolled in AleCardio after hospitalization for [acute coronary syndrome](#) – symptoms produced by a sudden blockage of blood flow to the heart – and screening to make sure their condition was stable. Median time from onset of symptoms to enrollment was 28 days.

A total of 7,226 patients, average age 61, were randomly assigned to aleglitazar at 150 µg daily or placebo. Although the design called for continuing treatment until 7,000 patients had been followed for 2.5 years and 950 primary endpoint events had been evaluated, the trial was cut short at 522 events. Heart failure, bone fractures and reversible renal issues are known for this class of drug, but researchers failed to find the hoped-for countervailing benefit in the main efficacy endpoint: time to death from cardiovascular cause or first non-fatal heart attack or stroke.

"The only unprecedented adverse effect was gastrointestinal hemorrhage, and none of the safety signals were overwhelming," said Michael Lincoff, M.D., director of C5Research, the Cleveland Clinic Coordinating Center for Clinical Research in Cleveland. "The issue was futility of cardiovascular superiority, with primary efficacy endpoints reached for 9.5 percent of aleglitazar group compared with 10 percent of the [placebo group](#)."

Heart failure did not reach a level of significant difference for the aleglitazar group but showed a strong trend at 3.4 percent compared with 2.8 percent for placebo. The gastrointestinal hemorrhage rate for aleglitazar was higher at a statistically significant 2.4 percent compared to 1.7 percent for the placebo group. The rate of reversible kidney events was significantly higher at 7.4 percent for aleglitazar compared to 2.7 percent for the placebo group. Bone fracture rates for the two groups were not significantly different.

In general, the study found no differences in heightened risk by patient characteristics that would make it possible to direct the drug safely to a specific subgroup. Increases in "good" HDL cholesterol and decreases in triglycerides were seen, along with small increases in "bad" LDL cholesterol.

"This study highlights the difficulty in predicting cardiovascular outcomes based upon beneficial effects on metabolic endpoints, particularly in agents that affect a complex spectrum of pathways and especially multiple-gene activators such as this one," Lincoff said. "This study may well mark the end of this class of drug being tested clinically."

More information: This study will be simultaneously published online in the *Journal of the American Medical Association* at the time of presentation.

Provided by American College of Cardiology

Citation: Higher risks without cardio benefits halt study of aleglitazar (2014, March 31) retrieved 9 April 2024 from <https://medicalxpress.com/news/2014-03-higher-cardio-benefits-halt-aleglitazar.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.