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Media Contacts Below

No Improvements with Losmapimod After Heart Attack

Drug aiming to reduce inflammation fails to meet endpoints, but may warrant further study

CHICAGO (April 4, 2016) — Patients taking losmapimod, an anti-inflammatory drug currently being developed, for 12 weeks following a heart attack did not show improvements in the trial's primary endpoint, the rate of cardiovascular death, subsequent heart attack or urgent coronary revascularization, which includes placement of a stent or coronary artery bypass surgery, according to research presented at the American College of Cardiology's 65th Annual Scientific Session.

The findings are from the initial phase of a losmapimod trial involving 3,500 patients. Because the trial failed to meet its primary endpoint, study authors said the second phase trial involving 22,000 patients will not go forward. However, in a finding that could warrant further study, the trial offers some evidence that the drug may benefit a subset of patients experiencing the most severe form of heart attack, ST-segment elevation myocardial infarction, or STEMI.

"Overall the results were neutral, showing no evidence of efficacy in our primary analysis," said Michelle O'Donoghue, M.D., a cardiologist and investigator in the TIMI Study Group at Brigham and Women's Hospital and the study's lead author. "We did, however, see intriguing signals toward there potentially being some efficacy in ST-elevation myocardial infarction patients. But because that signal was only within a smaller subgroup, we would need to validate those findings in a new study in order to confirm such an effect."

Although inflammation is a natural part of the body's response to injury, in some cases it can cause more harm than good. Inflammation is thought to increase cardiovascular risk after a heart attack by affecting the healing of heart muscle tissue, increasing the formation of plaque in the arteries and raising the likelihood that plaque will dislodge and cause another heart attack.

Losmapimod was developed to counteract these effects by inhibiting p38 mitogen-activated protein kinase, an enzyme present inside heart muscle cells and other cell types and that is activated by stressors such as a heart attack, heart failure or persistent high blood pressure. Earlier pilot studies involving several hundred patients suggested losmapimod could reduce inflammation in patients undergoing stenting procedures and hinted that it might help protect against major adverse cardiovascular events.

The new trial, LATITUDE-TIMI 60, the largest losmapimod study to date, was a randomized, double-blind staged phase 3 trial involving 3,500 patients hospitalized with an acute heart attack at 322 hospitals in 34 countries. Half of the patients received 7.5 milligrams of losmapimod twice daily and half received a placebo.

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After 12 weeks, a preliminary analysis showed no differences in rates of cardiovascular death, subsequent heart attack or urgent coronary revascularization among the group receiving losmapimod as compared to those receiving a placebo.

Although the trial was not large enough to conclusively demonstrate effects in specific patient subgroups, O'Donoghue said further study on losmapimod's effects in the heart may help to identify particular cases in which it could be beneficial.

"We are intrigued by the potential signal towards benefit, which was supported, at least in concept, by an earlier study that showed favorable effects in terms of left ventricular function following myocardial infarction. Thus, it remains possible that losmapimod may have favorable effects on healing of the heart after a heart attack, but that would require a separate study," O'Donoghue said.

In addition, other drugs designed to curb the inflammatory response may yet show promise.

"Although our study showed no efficacy, I think these results are not to say that we won't eventually find a therapeutic agent that targets pathways related to inflammation and shows clinical benefit. There are other trials that are ongoing that are targeting other inflammatory pathways, and the hope is that one of those compounds will demonstrate clinical efficacy," O'Donoghue said.

The study had a relatively small size and short duration. Enrolling more patients could potentially have put the study in a better position to more thoroughly evaluate the drug's effects, particularly in patient subgroups. It is also possible that taking the drug for more than 12 weeks would have yielded more benefits for patients. Further study would be required to address these limitations.

The trial was funded by GlaxoSmithKline.

This study was simultaneously published online in the *Journal of the American Medical Association* at the time of presentation.

The ACC's Annual Scientific Session, which in 2016 will be April 2-4 in Chicago, brings together cardiologists and cardiovascular specialists from around the world to share the newest discoveries in treatment and prevention. Follow @ACCMediaCenter and #ACC16 for the latest news from the meeting.

The American College of Cardiology is a 52,000-member medical society that is the professional home for the entire cardiovascular care team. The mission of the College is to transform cardiovascular care and to improve heart health. The ACC leads in the formation of health policy, standards and guidelines. The College operates national registries to measure and improve care, offers cardiovascular accreditation to hospitals and institutions, provides professional medical education, disseminates cardiovascular research and bestows credentials upon cardiovascular specialists who meet stringent qualifications.

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O'Donoghue will be available to the media in a press conference on Monday, April 4, 2016, at 9:30 a.m. CT/10:30 a.m. ET/2:30 p.m. UTC in Room N229.

O'Donoghue will present the study, "The Losmapimod To Inhibit P38 MAP Kinase As A Therapeutic Target And Modify Outcomes After An Acute Coronary Syndrome (LATITUDE-TIMI 60) Trial: Primary Results of Part A," on Monday, April 4, 2016, at 8 a.m. CT/9 a.m. ET/1 p.m. UTC in the Main Tent (North Hall B1).

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