



AMERICAN
COLLEGE of
CARDIOLOGY



58th Annual Scientific Session
MARCH 29-31 • ORLANDO

Embargoed for Release:
Sunday, March 29, 2009
2:00 p.m. EDT

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HIF-1- α OFFERS NO RELIEF FOR PERIPHERAL ARTERIAL DISEASE

Researchers to Go Back to the Bench to Learn More About This Intriguing Agent

Orlando, FL – A genetically engineered agent that researchers had hoped would stimulate the growth of new blood vessels in patients with clogged leg arteries gives patients no more relief than a placebo, according to research presented today at the American College of Cardiology's 58th annual scientific session. ACC.09 is the premier cardiovascular medical meeting, connecting cardiologists and cardiovascular specialists to the latest and most innovative findings in cardiovascular science.

Hypoxia-inducible factor-1 α (HIF-1 α) was unable to improve peak walking time in patients with peripheral arterial disease (PAD), nor increase the time patients could walk before experiencing leg pain, when compared to placebo.

“There was no demonstrable efficacy at any dose,” said Mark A. Creager, M.D., director of the Vascular Center at Brigham & Women's Hospital and a professor of medicine at Harvard Medical School, both in Boston. “I think there is a future for HIF-1- α , but we have to really go back to the bench and learn more about this agent's biology and the best way to deliver it.”

Peripheral arterial disease is both common and disabling. It is estimated to affect eight to 10 million people in the United States. Of these, as many as one-third experience symptoms, typically pain and cramps in the calf while walking. In severe cases patients have symptoms even at rest and face the possibility of amputation.

For many years there has been intense interest in developing treatments to stimulate the growth of new blood vessels in patients with blood- and oxygen-starved (ischemic) tissues. Hypoxia-inducible factor-1 α (HIF-1 α) has certain characteristics that made it both intriguing and promising. It naturally becomes more active in response to low tissue oxygen levels, plays a central role in orchestrating cellular responses to low oxygen levels, increases levels of vascular

growth factors, and has been shown in animal studies to promote blood vessel growth and blood flow in ischemic limbs. Early human studies also showed that HIF-1 α was safe when packaged in deactivated viruses and delivered by injection.

For the new study, researchers recruited 289 patients with claudication and PAD in both legs. Patients were randomly assigned to one of three doses of HIF-1 α or a saline placebo, administered in 20 injections to the thigh and calf muscle of each leg.

At the beginning of the study patients completed several treadmill exercise tests to establish a baseline peak walking time—the longest walking time they could endure—and claudication onset time—the time to the development of leg pain or cramps. The treadmill tests were repeated three and six months after treatment.

Peak walking time increased by about 30 percent in the placebo group and 23 percent to 35 percent in the HIF-1 α groups. The differences between groups were not statistically significant. Similarly there was no significant difference in claudication onset time, ankle-brachial index (a measure of the severity of PAD) or quality of life measurements among the four treatment groups.

“There is a tremendous need to identify therapies to improve the symptoms and quality of life in patients with claudication,” Creager said. “We’ll use this information and continue working. And whatever we learn in the leg will potentially be applicable to the heart as well.”

Dr. Creager will present the study “Treatment of Intermittent Claudication With Hypoxia-Inducible Factor-1 α ” on Sunday, March 29 at 2:51 p.m. in Hall A2.

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The American College of Cardiology (www.acc.org) works to influence health care policy and represents the majority of board certified cardiovascular care specialists through education, research, promotion, and the development and application of standards and guidelines. ACC.09 is the largest cardiovascular meeting, bringing together cardiologists and cardiovascular specialists to share the newest discoveries in treatment and prevention, while helping the ACC achieve its mission to address and improve issues in cardiovascular medicine.