Research offers new hope for peripheral artery disease sufferers

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Research led by vascular surgeons at Dartmouth-Hitchcock may offer new hope to sufferers of peripheral artery disease, the cause of nearly 60,000 lower-limb amputations annually, through the use of a patient's own stem cells.

Richard J. Powell MD, chief of vascular surgery at Dartmouth-Hitchcock, is the principal investigator on a national study – involving 550 patients at 80 sites around the country – of so-called "no option" patients, for whom the disease is so advanced that amputation is the only available treatment.

Powell's study is now in a three-year, third-stage clinical trial, after second-stage trials showed remarkable success at treating patients with CLI. The final results of the second-stage clinical trial have been published in the April, 2012, issue of *Molecular Therapy*.

Peripheral artery disease (PAD) afflicts more than 9 million patients in the United States. The condition results from blockages in blood vessels caused by atherosclerosis – hardening of the arteries – which can be a consequence of diabetes, high cholesterol, smoking, genetic predisposition, and other circumstances. In many cases, endovascular therapies such as insertion of stents or bypass surgery – similar to surgical processes used to treat blockages in the arteries of the heart – are used to reintroduce blood flow to the legs. But in about 150,000 patients with the most-severe forms of PAD, called critical limb ischemia or CLI, the disease is so extensive that endovascular therapy

isn't an option. That's where Powell's stem cell study comes in.

"All of us have stem cells in our bone marrow, and these stem cells can be utilized to repair other parts of our bodies," says Powell. "By taking the patient's own stem cells and injecting them into the ischemic leg, our hope is that we will then improve the blood flow in that part of the leg."

In the study, bone marrow is removed from the patient's hip, and then sent to a lab where stem cells are separated from the marrow and incubated over a two-week period, allowing more stem cells to grow. The stem cells are then re-injected intramuscularly into about 20 different spots on the patient's leg.

"We found that patients who received the stem cell therapy had a significantly lower incidence of amputation at six months than patients who received a placebo," said Powell.

After six months of the second-stage trials, approximately half of the patients who received a placebo died, required an amputation or saw their leg wounds worsen. Of those receiving the stem cell therapy, only a quarter died, required amputation, or saw their wounds worsen. Many showed significant improvement in blood flow in the ischemic limb.

"What was truly remarkable was that it was a relatively small number of patients, but that we saw clinically significant improvement in the stem cell-treated patients," he says. "It's compelling enough that there's no question that the pivotal trial needs to be done as quickly as possible."

The phase three trial has just begun, in which half of the patients will receive stem cell therapy and half will receive the placebo, measuring incidents of amputation or death one year after the treatment "We really want to see a therapy that's effective out to a year," says Powell. "Nonetheless, the results so far are really promising."

Provided by Dartmouth-Hitchcock Medical Center