

3. The non-technical abstract.

Lower limb intermittent claudication (IC), muscular pain with exercise relieved promptly by rest, is a disabling symptom affecting over 10 million patients in the United States. Intermittent claudication is caused by peripheral artery atherosclerosis, the same disease that causes heart attacks. Peripheral artery atherosclerosis impairs blood flow to skeletal muscles in the lower limbs. Growth factors, such as vascular endothelial growth factor (VEGF-A), have been shown in animal studies to improve blood flow to the lower limbs by promoting the growth of new blood vessels..

This clinical study tests the safety and feasibility of gene transfer of an agent (EW-A-401) intended to improve blood flow in the leg muscles of subjects with IC. The investigational agent is a circle of genetic material (plasmid DNA) that instructs the body to produce a genetically-engineered transcription factor, a special protein that regulates expression of genes. This specific transcription factor has been shown in animal studies to increase expression of the VEGF-A gene, and to promote the growth of new blood vessels. The study agent will be delivered by multiple injections into leg muscle during a single session. This is the first human experience using this particular transcription factor.

This study has a randomized, double-blind, dose-escalation, placebo-controlled design. The primary outcome measure will be safety and toxicity. In addition, we will collect exploratory effectiveness information including blood flow, walking capacity, quality of life, and inspection of blood vessels on samples of leg muscle.