Non-technical Abstract

The purpose of this clinical investigation is to determine if gene therapy can be used to cause the development of new blood vessels in legs with blocked arteries to increase blood flow and reduce leg pain at rest (*i.e.*, ischemic rest pain) in the feet or legs of patients with critical limb ischemia.

While angioplasty techniques and/or surgery may often increase blood flow in patients with blocked arteries sufficient to relieve rest pain, the blockages may in some cases be too extensive to permit either of these therapies. No medications are currently available that are likely to accomplish relief from rest pain. Accordingly, Vascular Genetics Inc. (VGI) is investigating the use of gene therapy as a treatment for increasing blood flow in legs with blockages that are too extensive to be treated surgically. This therapy has been previously tested in laboratory animals. The experiments suggested that if one performs surgery on the animal (rabbit) to create blockages in the leg arteries, one can use gene therapy to grow new blood vessels around the blockages. More recently, a similar approach using a closely related gene, has been employed successfully in a small group of patients with rest pain or nonhealing leg or foot ulcers.

The treatment will involve using a 27-gauge, 1.25-inch standard injection needle to deliver deoxyribonucleic acid (DNA), or genetic material, to one of the skeletal muscles of the diseased leg. Once inside the skeletal muscles, the DNA directs the cells of the skeletal muscles to make a certain protein called vascular endothelial growth factor-2 (VEGF-2). VEGF-2 is a protein that has been shown to cause new blood vessels to grow under a variety of conditions, including the above-described rabbit experiments. The DNA encoding vascular endothelial growth factor-1 (VEGF-1) protein, was used in the clinical gene therapy studies mentioned above that were previously conducted by Jeffrey M. Isner, M.D. VEGF-1 DNA and VEGF-2 DNA have been shown to cause very similar effects in animal experiments. The design of this proposed study is very similar to the design of the previous clinical studies with VEGF-1 DNA and to a clinical study conducted under Investigator IND BB-IND 7911.

VGI is thus investigating the possibility that, by using a needle to transfer the DNA for VEGF-2 to the leg with blocked arteries, new blood vessels will develop that will reduce pain and prevent further progression of the disease in patients with critical limb ischemia.