

AG-CLI-0205

Non-Technical Abstract

Critical leg ischemia (CLI) is the most severe manifestation of peripheral artery disease (PAD) in the legs with both high societal and individual patient costs. Current treatment options are inadequate, particularly for patients who are not candidates for replacement of blood vessels by surgery (revascularization), or in whom this procedure has failed. Even in patients who undergo surgical procedures to repair damaged arteries there remains a great need to improve the clinical outcome of limb preservation.

Therapeutic angiogenesis is the ability to promote the growth of new blood vessels for the treatment of disorders of inadequate tissue perfusion. AnGes, Inc. has begun investigating the hepatocyte growth factor (HGF) as a potential therapy for patients with CLI. HGF has potent angiogenesis activity that may result from a combination of direct effects on muscle and endothelial cells. AnGes' study agent (AMG0001) is a plasmid that contains the cDNA for human hepatocyte growth factor. The HGF Plasmid has demonstrated potential for promoting new blood vessel growth in damaged tissue based on *in vitro*, animal, and clinical studies.

The safety and effectiveness of HGF Plasmid is currently being investigated in a phase II, blinded, randomized, placebo-controlled study in more than 100 subjects with CLI. Subjects receive eight intramuscular injections of AMG0001 (0.4 or 4.0 mg) and/or placebo (saline) in one leg on days 0, 14 and 28. Enrollment for this study will be completed by the end of June 2005.

AG-CLI-0205 is a phase II, blinded, randomized, placebo-controlled study very similar in design to AG-CLI-0202. Subjects with CLI receive eight injections of AMG0001 or placebo on days 0, 14, and 28. The significant differences between AG-CLI-0205, compared to AG-CLI-0202, are: (1) 15 subjects will receive 4.0 mg of AMG0001 and 5 subjects will receive placebo, (2) each of the eight injections will contain 3 ml (instead of 2 ml) of solution, (3) eligible subjects must have a peripheral ischemic ulcer (which was allowed but not required in AG-CLI-0202), (4) duplex scanning will be used during the injection procedure to help identify the injection sites. Also, the precise anatomical locations of injections for each subject will be pre-determined by a central reader based on the screening angiogram. The effectiveness and feasibility of this method will be evaluated in order to design a phase III study.

The objectives of this study are to determine if AMG0001 intramuscular leg injections are safe and induce angiogenesis as determined by improved wound healing, reduction in amputation, improved pain at rest and improved hemodynamic measurements. The results of this study will provide insight into the response to AMG0001 treatment, possible mechanisms of action, and information useful in designing a phase III study.