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Vascular Disease

PHASE I STUDY OF MULTI-GENE CELL THERAPY IN PATIENTS WITH PERIPHERAL ARTERY DISEASE

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Background: Treatment options for patients with claudication due to lower extremity (LE) peripheral artery disease (PAD) are limited. Cell based therapies designed to induce angiogenesis are promising therapeutics that are intended to reduce pain and improve walking distance. We present the one year results of a Phase I safety, dose-escalating, non-randomized open label study, of MultiGeneAngio in subjects with claudication due to LE PAD.

Methods: A total of 12 subjects (4 cohorts of 3 patients each) were enrolled. Subjects received a single intra-arterial infusion of a suspension of equal amount of transduced autologous smooth muscle cells expressing vascular endothelial growth factor (VEGF165) and endothelial cells expressing Angiopoietin-1 (Ang-1) (Cohort 1 - 1 x 107, Cohort 2 - 2 x 107, Cohort 3 - 5 x 107, Cohort 4 - 7 x 107). The cell suspension was administered into the common femoral artery or its main branches proximal to the occlusion site of the more symptomatic LE, as indicated by a standardized treadmill test (Gardner protocol). The main outcomes were clinical safety and tolerability of MultiGeneAngio with laboratory measurements at specified time intervals compared to the baseline. Other measures included ankle-brachial index (ABI) and maximal walking time on treadmill testing.

Results: A total of 12 patients were successfully enrolled at 2 centers. All subjects were male, and their mean age was 60 ± 5 years. Historical factors included diabetes (25%), hyperlipidemia (92%), hypertension (92%), CAD (75%), COPD (33%), and smoking history (92%). At the one-year post treatment, no serious adverse events (SAEs) related to MultiGeneAngio were observed. Safety endpoints including VEGF and Ang-1 plasma protein levels were within normal ranges in all subjects. Mean maximal walking time increased from baseline to 1 year (345 to 533 seconds; $p < 0.05$), index limb ABI was unchanged (0.58 to 0.61, p = ns).

Conclusions: MultiGeneAngio, an autologous, transduced, cell based therapy was well tolerated and safe in this phase-1 study. The therapy was also associated with increased walking time in these patients with LE claudication. The results of this study warrant further randomized human studies.