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AnGes MG, Inc.

Phase I clinical trials of HGF plasmid for the treatment of Ischemic Heart Disease (IHD) underway in the United States
-- Clinical trials of HGF plasmid for both peripheral arterial disease (PAD) and IHD --

AnGes MG prepared for Phase I clinical trials of HGF plasmid for IHD through AnGes Inc. (its US subsidiary), and has now started Phase I clinical trials. The first round of trials was initiated on November 23, 2004.
AnGes MG has also been conducting Phase II trials of HGF plasmid for PAD in the USA since April 2003. AnGes MG has started clinical trials for IHD, which affects a larger number of patients. AnGes MG intends to market HGF plasmid for both PAD and IHD at an early date.

HGF plasmid contains the gene for human hepatocyte growth factor (HGF), which has the ability to generate the growth of new blood vessels. This neovascular effect is intended to alleviate ischemic disease, in which the lumen of the blood vessel is narrowed due to arteriosclerosis and the blood flow in the heart is impaired. As this gene medicine operates in a different manner than conventional drugs, it is expected to be effective for people who do not sufficiently respond to conventional drug therapy or who cannot undergo surgery. AnGes is developing HGF plasmid for indications related to PAD, in which blood circulation in the lower limbs is decreased and IHD, in which blood flow in the heart is impaired.

The clinical trials started at this time are Phase I clinical trials of HGF plasmid for the treatment of IHD in the USA. Healthy volunteers are often used as subjects in these trials to evaluate safety. However, for anticancer and gene medicines for which it is deemed inappropriate from a safety standpoint to administer them to normal, healthy individuals, Phase I trials are conducted using subjects with the target disease. In the clinical trials for IHD being conducted at this time, AnGes MG will be using a limited number of patients with severe ischemic heart disease as subjects to evaluate the safety, efficacy and practicality of the treatment, because HGF plasmid is a gene medicine, and because it will be administered directly to ischemic cardiac muscle using a catheter. AnGes MG is also making preparations for starting clinical trials in Japan as soon as possible following the start of Phase I clinical trials for IHD in the USA.

AnGes Inc. is also now conducting U.S. Phase II clinical trials using HGF plasmid for the treatment of PAD. In Japan, AnGes MG is currently conducting PAD-related multi-center double blind Phase III clinical trials. With the start of clinical trials for IHD, the Group intends to market HGF plasmid as a gene medicine for both PAD and IHD in Japan, the USA and Europe.

AnGes MG has granted Daiichi Pharmaceutical Co., Ltd. the distribution rights for HGF plasmid in both the PAD and IHD indications in Japan, the USA and Europe.

Reference

Current Pipeline for HGF Plasmid Therapeutic Agents

Field	*Region*	*Development Phase*	*Licensee*
Peripheral arterial disease	Japan	Phase III	Daiichi Pharmaceutical Co., Ltd.
	USA	Phase II	
Ischemic heart disease	USA	**Phase I**	
Parkinson's disease		Pre-clinical level	Undecided

Note: The underlined item has been revised.

Therapeutic significance of HGF plasmid -

It is known that HGF has a strong vascularizing effect. HGF plasmid (the first genetic medication to be produced in Japan) deposits a gene to produce HGF in sites where vascular necrosis occurs. Generation of HGF protein locally, promotes the blood vessel regeneration to improve the (arteriosclerotic) condition. This agent does not employ a virus vector to introduce the genetic sequence to a patient's DNA; since it is a pure, "naked" DNA sequence, negative effects that usually accompany a DNA sequence introduction with a virus vector do not appear here. Moreover, since HGF plasmid alters the condition of necrosis by regenerating blood vessels, as opposed to all conventional pharmacological agents, positive results can be expected in cases when conventional therapy for PAD and IHD fails, or is increasingly complicated.