



Vascular Disease

Overview

Vascular diseases are disorders that affect the extensive network of blood vessels in the body, leading to life and limb threatening disorders, such as critical limb ischemia, stroke, kidney failure, gangrene and abdominal aortic aneurysms. The disorders can affect any of the blood vessel types in the vascular system, namely arteries, veins, lymphatics and capillaries.

Peripheral vascular disease (PVD) or peripheral artery disease (PAD) affects the peripheral arteries and veins that carry blood to and from arm and leg muscles, organs in and below the stomach area, and also the arteries leading to the head.¹ When PVD occurs in the arteries outside the heart, it may be referred to as PAD. However, the terms “peripheral vascular disease” and “peripheral artery disease” are often used interchangeably.

PVD is one of the most common vascular diseases that affects one in three people over the age of 70. About eight to twelve million people are affected in the United States, with disease prevalence increasing with age.² Changes in these vessels disturb the normal flow of blood. Such changes include atherosclerosis, or the hardening of the arteries, which is caused by the buildup of fat and cholesterol depositions on their inside walls. This buildup narrows the vessels and causes ischemia, the inadequate blood

(and thus oxygen) flow to the body's tissues.³ Critical limb ischemia (CLI) is the most severe form of PVD caused by chronic inflammatory processes associated with atherosclerosis. There are estimated to be over 1 million people in the United States with CLI.⁴

PVD can also manifest itself in venous blood clots (like in deep vein thrombosis), inflammation and swelling. Venous blood clots are also a common ailment for many Americans, with 2.5 million people suffering from such clots in the leg veins every year.⁵

Lifestyle choices and heredity play large factors in the development of vascular diseases. Age, high blood pressure, smoking, obesity, high cholesterol, diabetes, family history and sedentary lifestyle are all risk factors for the diseases.⁶

Vascular Disease and Regenerative Medicine

Several cell-based regenerative medicine technologies targeting certain types of vascular disease, including PAD and CLI, are in mid- to late-stage clinical development.

Aastrom is developing an autologous ixmyelocel-T cell therapy, a patient-specific, expanded multicellular therapy that selectively amplifies mesenchymal cells, monocytes and macrophages. They are currently testing the

effectiveness of this therapy in two clinical trials for CLI. The lead trial is in Phase 3, and assessing the effect of treatment with ixmyelocel-T on amputation-free survival patients at 12 months post-injection, while the other is a Phase 2 trial to assess the safety and efficacy of the therapy.

Cytomedix is developing an autologous stem cell product ALD-301, a population of stem cells isolated from the patients' bone marrow which express high levels of the enzyme ALDH, an indicator of biological activity in heterogeneous early stage stem cells. In a Phase 1/2 trial of their product for CLI, ALD-301 demonstrated good tolerability and provided initial evidence of increased blood flow and improved clinical status for patients in the treatment group. Cytomedix is collaborating with NIH on a Phase 2 clinical study in patients with intermittent claudication (IC) which is caused by PAD.

Juventas Therapeutics' lead product JVS-100, a biologic-based regenerative therapeutic that encodes stromal cell-derived factor-1, is also targeting ischemic injury. The cytokine stimulates a number of protective anti-inflammatory pathways, causes the down regulation of pro-

inflammatory mediators and can also prevent cell death. Furthermore, SDF-1 recruits stem cells to the site of tissue damage, which promotes tissue preservation and blood vessel development. The company is currently enrolling patients in a Phase 2 study for CLI patients.

Pluristem's patented PLX (Placental eXpanded) placenta-derived stem cells are being used in a multi-national study of peripheral artery disease. Pluristem completed clinical follow up in two Phase 1/2a studies in CLI that indicated that PLX-PAD was safe and potentially effective for the treatment of patients with CLI. In January 2013, the company announced it was expanding its Phase 2 study of PLX-PAD cells in patients with IC.

Tissue Genesis is developing a treatment for vascular disease using an adipose (fat)-derived stem cell-coated vascular graft. This treatment utilizes Tissue Genesis' Cell Isolation System, a compact, automated desktop unit that utilizes liposuctioned adipose tissue to isolate millions of adult stem cells in about one hour. In April 2011, the company began enrolling patients in an FDA-approved clinical trial for PVD.

Vascular Disease: Economic Impact



\$164–290 Billion

Healthcare cost for Americans suffering from PAD and related conditions in 2010⁷



\$21 Billion

Vascular-related hospitalization for PAD alone in the U.S.⁸

¹ "Peripheral Vascular Disease," St. Luke's Episcopal Hospital website, www.stlukeshouston.com/OurServices/HeartCareServices/Peripheral_Vascular_Disease.cfm

² "Vascular Disease Statistics," Vascular Disease Foundation website, <http://vascular-disease.org/education-prevention/knowledge-is-power/vascular-disease-statistics/>

³ "About Vascular Diseases," Pacific Vascular, Inc. website, www.pacificvascular.com/vascular-disease.htm

⁴ "CLI Clinical Trials: Advancing stem cell therapy to treat critical limb ischemia," Aastrom Biosciences website, www.aastrom.com/clinical-research/cli-clinical-trials/

⁵ "Vascular Disease Statistics," Vascular Disease Foundation website, <http://vascular-disease.org/education-prevention/knowledge-is-power/vascular-disease-statistics/>

⁶ Stony Brook Medicine, "Vascular Disease," Stony Brook University website, <http://stonybrookmedicine.edu/patientcare/vascular-disease>

⁷ "In Recognition of National Peripheral Artery Disease (PAD) Awareness Month, The Sage Group Comments on the Economic Burden of the Disease," Sage Group press release, September 8, 2011, on the Business Wire website, www.businesswire.com/news/home/20110908006722/en/Recognition-National-Peripheral-Artery-Disease-PAD-Awareness

⁸ University of Minnesota School of Public Health, "Peripheral artery disease continues to drive escalating health care costs in the United States," University of Minnesota website, www.health.umn.edu/media/releases/PAD/index.htm