Groundbreaking Myasthenia Gravis Cellular Therapy Study Published in Lancet Neurology

A new study led by two neurologists at the University of Miami Miller School of Medicine points to a potential novel form of CAR T cellular therapy for myasthenia gravis (MG), a chronic autoimmune disorder characterized by muscle weakness. The study findings were recently published in the British journal Lancet Neurology, along with an accompanying commentary highlighting the importance of this innovative approach to the treatment of a condition for which there is no cure.

Microscopic image of thymoma, a tumor of the thymic gland, show necrotic material admixed with lymphocytes, myasthenia gravis.

Volkan Granit, M.D., M.Sc., a clinical researcher at the University of Miami, was the co-first author of the collaborative study, “Safety and Clinical Activity of Autologous RNA Chimeric Antigen Receptor T-cell Therapy in Myasthenia Gravis (MG-001): A Prospective, Multicentre, Open-Label, Non-Randomised Phase 1b/2a Study.”

The commentary in Lancet Neurology, “Are CAR T Cells the Answer to Myasthenia Gravis Therapy?” was written by Andreas Meisel, M.D., chief executive director, Center for Stroke Research Berlin.

“The innovative approach builds upon advances in cancer immunotherapy to administer a first-of-its-kind RNA-engineered chimeric antigen receptor [rCAR T] cells in a small group of patients with myasthenia gravis,” said Dr. Granit. “Although highly effective, the toxicity of conventional CAR T-Cell therapies limits their use in diseases beyond cancer. The novel cell design employed in this study offers a significant improvement in safety and tolerability.”

Descartes-08 Treatment

The treatment, labeled Descartes-08, targets the b-cell maturation antigen (BCMA), a protein that is selectively expressed in plasma cells, said Dr. Granit. By targeting the plasma cells, Descartes-08 addresses a key step of the disease process in MG. Descartes-08 is a personalized (autologous) cell therapy during which cells are collected from a patient, engineered with RNA, and returned to the same individual in an outpatient setting.

This proof-of-concept study enrolled 14 patients with MG at eight sites in Florida, California, Oregon and North Carolina, who received six weekly, twice weekly, or monthly infusions.

“Beyond the apparent safety and tolerability, there were also promising signs of improvement on MG severity scales that continued through nine months of follow-up monitoring,” said Dr. Granit.

Dr. Granit and co-first author, Michael Benatar, M.D., Ph.D., professor of neurology, the Walter Bradley Chair in ALS Research and executive director of the Amyotrophic Lateral Sclerosis (ALS) Center of the University of Miami Miller School of Medicine, collaborated with Cartesian
Therapeutics for the design of the study. Funding was provided by the sponsor and by the NIH’s National Institute of Neurological Disorders and Stroke (NINDS).

**Sylvester Provides World’s First rCAR-T Therapy for MG Patient**

Calling the study “a testament to interdisciplinary collaboration,” Dr. Granit thanked Sylvester Comprehensive Cancer Center oncologist Denise Pereira, M.D., assistant professor of clinical medicine; Krishna Komanduri, M.D., former professor and chief, Division of Hematology and Oncology; and Cara Benjamin, Ph.D., director of the Cellular Therapy Laboratory, for their partnership.

“Dr. Pereira and her team at Sylvester were extremely generous with their time and expertise in providing the first rCAR-T therapy to an MG patient in the world,” Dr. Granit said. “Julie Steele, R.N., the neuromuscular clinical trials manager in the Department of Neurology, played an invaluable role in the study conducted at the UM.”

“This study is an example of how a deeper understanding of the immunobiology of myasthenia gravis is driving the development of innovative therapeutic approaches to the treatment of this chronic autoimmune disorder,” said Dr. Benatar.

A randomized, placebo-control follow-up study to further test the safety and efficacy of Descartes-08 in patients with MG is ongoing.

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