New Therapy Found For Rare Lung Disorder

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DENVER — Researchers at National Jewish Health and several other institutions are reporting the first successful trial of a medication to treat lymphangioleiomyomatosis (LAM), a rare and deadly disease that strikes almost exclusively young and middle-age women. They report in the March 16, 2011, online version of The New England Journal of Medicine that the FDA-approved drug sirolimus halted lung-function-loss in LAM patients.

“This is a textbook case of successful bench-to-bedside science,” said co-author Kevin K. Brown, MD, Professor of Medicine at National Jewish Health. “Basic scientific discoveries have been translated into medications, bringing the first effective medical therapy to women with LAM.”

LAM is a progressive, cystic lung disease. In LAM, an unusual type of smooth-muscle cell grows uncontrollably and spreads from an unknown source to restricted areas in the body, including the lungs, lymph nodes and vessels and kidneys, limiting the flow of air, blood and lymph.

Shortness of breath and recurrent lung collapse are common in patients with LAM. Many patients die of respiratory failure. Median survival of the disease from onset of symptoms is 8-10 years. Until now, lung transplantation has been the only hope for patients who progress to respiratory failure.

Basic research, funded by the LAM Foundation, revealed in 2000 that a genetic abnormality and signaling pathway, known as mTOR, are involved in the disease. Sirolimus, also known as rapamycin, used widely in the treatment of a variety of cancers and as an immnosuppressive agent, inhibits activation of the mTOR pathway.

The current study, known as the Multicenter International LAM Efficacy of Sirolimus, or MILES, trial was the first randomized, controlled study designed to develop a therapy for this life-threatening illness.
A total of 89 patients with LAM were enrolled in the United States, Canada and Japan. Patients were randomly assigned to either receive sirolimus or a matched placebo.

During a year of treatment patients taking placebo experienced an average loss of FEV1 (forced expiratory volume in one second) of 12 milliliters per month. Patients taking sirolimus held essentially constant in their FEV1. The active treatment was also associated with improvement in measures of functional performance and quality of life.

“Sirolimus essentially halted lung-function decline among LAM patients,” said co-author Gregory Downey, MD, Professor of Medicine, Immunology and Pediatrics at National Jewish Health. “Unfortunately lung function began declining once patients stopped taking the medication.”

“LAM is typically slowly progressive, and sirolimus therapy has risks, so treatment decisions should be individualized,” said Francis X. McCormack,MD, lead author and Professor of Medicine at the University of Cincinnati. “Also, additional trials are needed to determine the optimal dose and duration of treatment with sirolimus. Given the toxicity profile of the drug during a one-year period, the long-term safety of this approach over an extended course must be carefully evaluated.”

Dr. McCormack led the effort, which included researchers with National Jewish Health and more than a dozen other institutions including Cincinnati Children’s Hospital Medical Center; the University of Toronto, Canada; the University of Texas Health Science Center at Tyler; the University of California at Los Angeles; Oregon Health and Science University, Portland; Niigata University Medical & Dental Hospital, Japan; National Hospital Organization Kinki-Chou Chest Medical Center, Osaka, Japan; the National Heart, Lung, and Blood Institute, Bethesda; Medical University of South Carolina, Charleston; the Cleveland Clinic Foundation; and Brigham and Women's Hospital, Boston.

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National Jewish Health is known worldwide for treatment of patients with respiratory, cardiac, immune and related disorders, and for groundbreaking medical research. Founded in 1899 as a nonprofit hospital, National Jewish Health remains the only facility in the world dedicated exclusively to these disorders. Since 1998, *U.S. News & World Report* has ranked National Jewish the #1 respiratory hospital in the nation.

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