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Media Advisory

Scientists at The Scripps Research Institute Demonstrate that Powerful Anti-Lymphocyte Drug Favorably Influences the Course of Chronic Progressive MS

Cladribine shows promise as a therapy for the disorder.

What: A team of researchers led by Ernest Beutler, M.D., has reported in this week's issue of The Lancet that Cladribine, or 2-chlorodeoxyadenosine (2-CdA), a powerful anti-lymphocyte drug developed and tested at The Scripps Research Institute (TSRI), has been shown to favorably influence the course of chronic progressive multiple sclerosis (MS) and shows promise as a therapy for the disease.

The use of the drug for MS was considered by scientists after extensive experience with the drug in the successful treatment of lymphoid leukemias, particularly hairy cell leukemia.

Who: Dr. Beutler is Chairman of the Department of Molecular and Experimental Medicine at TSRI and a member of the National Academy of Sciences. Additional authors of the study, entitled "Effectiveness of Cladribine in the Treatment of Chronic Progressive Multiple Sclerosis," are Jack C. Sipe, M.D., Division of Neurology, Scripps Clinic; John S. Romine, M.D.,
Background: Multiple sclerosis affects approximately 300,000 people in the U.S. Of these, upwards of one-half suffer from chronic progressive multiple sclerosis, a severely disabling disease of the central nervous system that involves the destruction of the insulating sheath, or myelin, that covers the nerve fibers. Muscle coordination, visual sensation and other signals are slowed or blocked. Patients with the disease suffer from fatigue, difficulty walking, spasticity, muscle weakness, tremor and impaired thinking and reasoning. Some patients develop complete paralysis.

While the cause of MS is unknown, many researchers believe that autoimmune mechanisms play an important role, theorizing that white blood cells of the immune system attack the myelin sheath that insulates the nerves. Cladribine was tested in this study to determine whether selective lymphocyte depletion could slow or halt clinical disease progression and allow patients to improve.

The Study: Forty-eight chronic progressive MS patients participated in a double-blind, placebo-controlled study of the effectiveness of 2-CdA administered by central venous catheter. Patients were paired by age, sex, duration and severity of the disease. Twenty-four patients were randomized to four

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monthly infusions of the drug, while the other 24 were given saline solution. Because of the positive results at one year, the formal study was terminated and the placebo group was treated with one-half the dose of 2-CdA given to patients during the first year of the study.

At monthly examinations, the patients' levels of neurologic disability were measured by standard rating scales. In addition, the spinal fluid was tested to measure immune activity and the volume of brain lesions was determined by magnetic resonance imaging initially and at six, 12, 18 and 24 months.

Cladribine use was associated with a highly significant difference in neurologic rating scores. The neurologic status of patients given Cladribine was slightly improved or stabilized; patients given the placebo continued to manifest a decline of neurologic status. Further, the total volume of MS brain lesions decreased in patients treated with Cladribine. In addition, there was a significant difference in the spinal fluid findings of patients receiving Cladribine and those receiving the placebo, suggesting decreased autoimmune activity in response to Cladribine.

A multi-center trial will be implemented soon under the leadership of the Scripps group. This trial will make the experimental treatment available to eligible patients in various parts of the country.

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