EMBARGOED
by the American Academy of Neurology
until Thursday, May 5, 1994, 12:00 noon EDT


CLADRIBINE FAVORABLY ALTERS THE CLINICAL COURSE OF PROGRESSIVE MULTIPLE SCLEROSIS

Washington, D.C. May 5, 1994 — A powerful anti-lymphocyte drug developed and tested at The Scripps Research Institute in La Jolla, Calif., has been demonstrated to favorably influence the course of chronic progressive multiple sclerosis (MS) and shows promise as a therapy for the disorder.

The use of Cladribine, or 2-chlorodeoxyadenosine (2-CdA), in the treatment of multiple sclerosis was considered by the researchers after extensive experience with the drug in the successful treatment of lymphoid leukemias, particularly hairy cell leukemia. In a large study conducted at Scripps in 1990, 146 hairy cell leukemia patients were given a single dose of 2-CdA and 86% achieved a complete remission.

Multiple sclerosis affects approximately 300,000 people in the United States. Of these, about one-half to one-third suffer from chronic progressive multiple sclerosis, a severely disabling disease of the central nervous system which 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 MORE
fatigue, difficulty walking, spasticity, muscle weakness, tremor, and impaired thinking and reasoning. Some patients develop complete paralysis.

While no one is certain of the cause of MS, many scientists believe that autoimmune mechanisms play a role, theorizing that the 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.

Jack C. Sipe, M.D., Head of the Division of Neurology at Scripps Clinic, presented the results of the clinical trial today at the annual meeting of the American Academy of Neurology in Washington, D.C. The title of the presentation was, "Cladribine Favorably Alters the Clinical Course of Progressive Multiple Sclerosis." The results also have been submitted to a major medical journal for publication.

According to Dr. Sipe, "Immunosuppressive therapy has previously been used in patients with multiple sclerosis, but none of the prior treatments approach in efficacy the results that we have seen with Cladribine. It has shown a stabilizing effect on the neurologic status of the MS patients who were studied. We are looking forward to obtaining results from a multi-center trial which is in the planning stages."

Ernest Beutler, M.D., Chairman of the Department of Molecular and Experimental Medicine and co-developer of 2-CdA, organized and led the multidisciplinary team that performed these studies. He explains, "There is no question that Cladribine favorably influences the clinical course of chronic progressive multiple sclerosis. It is an immunosuppressive drug with potential side effects and long-term toxicity that may as yet
be unknown. Therefore, the advisability of using this drug in the treatment of MS needs to
be established in large clinical trials which are now being planned."

This major study was performed with grants of more than $3 million from the General
Clinical Research Center of the National Institutes of Health (NIH), the Neurologic
Disease Institute of the NIH, the Orphan Drug Branch of the Food and Drug
Administration, and the Sam and Rose Stein Charitable Trust Fund.

In 1990, Drs. Beutler and Sipe treated four patients with six monthly doses of 2-CdA, with
clear evidence of improvement both clinically and as evidenced by increased performance
on a generally accepted neurologic rating scale. Encouraged by these results, they designed
the current study with the collaboration of James A. Koziol, Ph.D., biostatistician in the
Department of Molecular and Experimental Medicine; John S. Romine, M.D., Division of
Neurology; Robert McMillan, M.D., Division of Hematology and Oncology; and Jack
Zyroff, M.D., Division of Neuroradiology.

Forty-eight chronic progressive MS patients participated in a double-blinded, 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 monthly infusions of 2-CdA while the other 24 were given saline
infusions. 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, twelve, eighteen and twenty-four months.

Cladribine administration 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.

Generally, the drug was well tolerated, but a few problems were encountered in the study, including low platelet counts in four patients. Also, one patient developed bone marrow suppression from which she completely recovered within six months. One patient died from acutely acquired hepatitis B, an event not considered by the scientists to be related to 2-CdA.

A multi-center trial soon will be implemented under the leadership of the Scripps group. This trial will make the experimental treatment available to eligible patients in various parts of the country. Patients are being screened for the study and may call 1-800-SCRIPPS for more information.

###

Ernest Beutler, M.D., may be reached at the Omni Shoreham Hotel, room 315, tel: (202) 234-0700, Tuesday, May 3, in the afternoon; Wednesday, May 4; and Thursday, May 5, in the morning.