Ongoing Evaluation of the Safety and Efficacy of Mitoxantrone in Multisite Sclerosis: The RENEW Study

Victor R. Zivin, Ahmad Al-Sabbagh, Randy Bennett, Patricia Coyle, Daniel Mikul, Hillie Pantich, Edward Fox, Loren Rotak, William Sheremata, Stanton Elias

Baylor College of Medicine, Houston, TX, USA; EMD Serono, Rockland, MA, USA; Stony Brook University Hospital/Stony Brook, NY, USA; University of Michigan, Ann Arbor, MI, USA; Fletcher Allen Health Care, Burlington, VT, USA; "Central" Texas Neurology Consultants, Round Rock, TX, USA; Marshfield Clinic, Marshfield, WI, USA; Multiple Sclerosis Center, University of Miami School of Medicine, Miami, FL, USA; Department of Neurology, Henry Ford Health Science Center, Detroit, MI, USA

Introduction and Purpose

- Multiple sclerosis (MS) is a chronic disease affecting the central nervous system that can ultimately lead to severe neurologic disability.
- The immunomodulatory agent mitoxantrone has been approved for the treatment of patients with worsening relapsing-remitting MS (RMSRs), progressive-relapsing MS (PRMS), or secondary-progressive MS (SPMS) whose neurologic status is significantly different below relapses.
- The Registry to Evaluate Novembrine Effects in Worsening Multiple Sclerosis (RENEM) is a multicenter, open-label, observational study designed to evaluate the safety of mitoxantrone therapy in patients with worsening MS. Patients are monitored for 2-3 years during treatment and for 3-2 years during the follow-up phase, for a total of more than 6 years during treatment and follow-up. The first patient reached the 6-year mark in March 2008, and the last patient will reach 6 years in January 2013.
- Objectives of the ongoing RENEW study are to:
  - Evaluate the long-term effects of mitoxantrone on cardiac function
  - Evaluate the acute hematologic toxicity of mitoxantrone as manifested by serious infections complications
  - Evaluate the occurrence of serious adverse events (SAE) data
  - Determine the distribution of cumulative mitoxantrone doses administered
  - Determine cumulative mitoxantrone doses administered
  - Determine the rate of discontinuation of mitoxantrone therapy
  - Data have been collected on an ongoing basis since commencement of the study. The previous reporting periods included data gathered and validated through January 16, 2008.
  - This poster presents cumulative validated data from the beginning of the study in April 2001 through the recent reporting period, ending on January 15, 2008.

Methods

- A total of 503 patients with MS receiving mitoxantrone were enrolled at 46 centers across the United States.

Inclusion Criteria

- Patients were eligible for the study if they had a defined or laboratory-supported diagnosis of RMSRs, PRMS, or SPMS and had initiated mitoxantrone (12 mg/m² treatment) within 3 months of the institutional Review Board approval.
- As indicated in the study protocol, all patients are expected to follow the dosing and monitoring recommendations specified in the medication package insert.
- Additional entry criteria for the study included age 18-65 years, plateau count 100,000 cells/μL, and granulocyte count ≥ 5000 cells/μL.

Exclusion Criteria

- Had primary-progressive MS, a history of congestive heart failure (CHF), or heart failure, pulmonary edema, and other cardiovascular dysfunction (CHF, CHF).
- Had received previous treatment with mitoxantrone, other immunosuppressive or methotrexate, methotrexate, or total lymphocyte depletion (TLD).
- Present with any of the following: transient or transiently transient (< 2 standard deviations above the mean) for age-related measures or to be strongly suggested by the preliminary data.