(S04) ACUTE LEUKEMIA IN MULTIPLE SCLEROSIS PATIENTS TREATED WITH MITOXANTRONE
A. Al-Sabbagh,1 D. Dawson,2 R. Bennett,1 F. Dangond1

1Medical Affairs, EMD Serono, Inc, Rockland, MA; 2US Product Surveillance and Quality Assurance, EMD Serono, Inc, Rockland, MA

Background: Leukemia secondary to mitoxantrone treatment has been reported in patients with multiple sclerosis (MS). The package insert for Novantrone (2009) includes data from one cohort study (N = 802) and one safety and tolerability monitoring study (N = 509) that report the postmarketing incidence of leukemia to be 0.25% and 0.60%, respectively. Other published studies have suggested even higher incidences. Objectives: To assess and describe the US postmarketing reports of acute leukemia following treatment with Novantrone (mitoxantrone for injection concentrate) in patients with MS. Methods: Case reports of acute leukemia following mitoxantrone therapy in MS patients, including three cases from the Registry to Evaluate Novantrone in Worsening MS (RENEW), were compiled and submitted to EMD Serono, Inc, between March 2003 and April 2009. Results: A total of 44 cases of acute leukemia secondary to mitoxantrone therapy were identified. Complete patient characteristics were not available for all cases. Women accounted for 70% (31/44) of patients, and the median age was 49 years (range, 29–68; n = 41). Patients received a mean cumulative dose of mitoxantrone of 84.9 mg/m² (SD = 23.1; range, 48–135; n = 20), and the median time to leukemia onset after stopping mitoxantrone therapy was 17 months (range, 0–60; n = 32). Acute myelogenous leukemia and its subtype, acute promyelocytic leukemia, were the most common types of leukemia observed in this analysis, reported in 17 (38.6%) and 16 (36.4%) patients, respectively. Other reports included leukemia and secondary leukemia not otherwise specified (n = 7; 15.9%), chronic myeloid leukemia (n = 2; 4.5%), pre–B cell acute lymphoblastic leukemia (n = 1; 2.3%), and myelodysplasia (n = 1; 2.3%). The incidence of any type of leukemia did not appear to be related to the dose of mitoxantrone. Data were previously presented at the 2010 American Academy of Neurology Annual Meeting. Conclusions: The risk of leukemia secondary to mitoxantrone therapy may be significant in patients with MS. Although the exact incidence has yet to be established, the possibility of this adverse event warrants ongoing investigation and monitoring of patients receiving mitoxantrone for MS.

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