(S28) CARDIOVASCULAR ADVERSE EVENTS WITH MITOXANTRONE: RENEW STUDY RESULTS

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Background: Mitoxantrone has been associated with cardiotoxicity, which may occur at any time during treatment or months to years after discontinuation. Objectives: To characterize cardiovascular adverse events with Novantrone (mitoxantrone for injection concentrate) treatment over 5 years from the Registry to Evaluate Novantrone Effects in Worsening Multiple Sclerosis (RENEW) study. Methods: Patients with secondary progressive, progressive relapsing, or worsening relapsing-remitting multiple sclerosis (MS) enrolled in this prospective, open-label, multicenter, phase 4 observational trial. Intravenous infusion of mitoxantrone 12 mg/m² was administered on a quarterly basis until patients reached a cumulative dose of 140 mg/m² or treatment was discontinued. Cardiovascular assessments included left ventricular ejection fraction (LVEF; monitored after every dose), symptoms of congestive heart failure (CHF), and cardiac-related events considered serious (SAEs). Patients were assessed at baseline, every 3 months during treatment, and annually after treatment discontinuation for up to 5 years (observational period [OBS]). Results: The 5-year trial was completed by 172 (33.8%) of the 509 patients who enrolled and received at least one dose of mitoxantrone. The mean treatment duration was 1.5 years, and patients achieved a mean cumulative dose of 69.8 mg/m². An LVEF ≤50% of baseline was reported in 27 of 509 (5.3%) patients during treatment and 14 of 250 (5.6%) patients during OBS. Symptoms of CHF were reported by 10 of 509 (2.0%) patients (treatment phase, 6; OBS, 4). Cardiac-related AEs were reported by 25 of 509 (4.9%) patients (treatment phase, 22; OBS, 4), with reduced LVEF being the most common SAE. Two cardiac-related deaths occurred in this study, including cardiomyopathy/CHF/reduced LVEF (n = 1) and cardiorespiratory arrest (n = 1). Additional data from a post hoc analysis, assessing potential contributing factors to cardiotoxicity, will be shown. Conclusions: As stated in the Novantrone package insert, mitoxantrone may result in cardiac dysfunction in some patients, including reduced LVEF or irreversible CHF. Clinical monitoring for cardiac adverse events is important both during mitoxantrone treatment and after discontinuation.

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