

Abstract
Mitozolomide (NSC-353451; CCRG 81010; M and B 39565) is a novel potential anticancer agent that was selected for phase I study on the basis of broad spectrum activity in mouse tumors. Initially, mitozolomide was given iv as a short infusion to 37 patients in doses ranging from 8 to 153 mg/m2. Nausea and vomiting was dose-related but was not severe. The dose-limiting toxic effect was thrombocytopenia at doses greater than 115 mg/m2, and recovery from the thrombocytopenia was delayed up to 8 weeks. Partial responses were seen in two patients with adenocarcinoma of the ovary. The pharmacokinetics of mitozolomide showed that the half-life of the intact drug in the plasma was between 1 and 1.3 hours. The area under the curve was proportional to the dose administered. Mitozolomide is well-absorbed; therefore, future studies are recommended using a single-dose schedule orally or iv. In the phase I study reported here, a dose of 115 mg/m2 appeared to be safe, but additional studies have shown that when given orally to an older population, most patients experienced thrombocytopenia less than 50,000 cells/mm3. The recommended dose using current data is 90 mg/m2 iv or orally.

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