ABSTRACT

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Nanoliposomal Irinotecan and Metronomic Temozolomide for Patients With Recurrent Glioblastoma: BrUOG329, A Phase I Brown University Oncology Research Group Trial.

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BACKGROUND: Liposomal formulations may improve the solubility and bioavailability of drugs potentially increasing their ability to cross the blood-brain barrier. We performed a phase I study to determine the maximum tolerated dose and preliminary efficacy of pegylated nanoliposomal irinotecan (nal-IRI)+metronomic temozolomide (TMZ) in patients with recurrent glioblastoma.
PATIENTS AND METHODS: Patients with glioblastoma who progressed after at least 1 line of therapy were eligible. All patients received TMZ 50 mg/m^2/d until disease progression. Three dose levels of nal-IRI were planned, 50, 70, and 80 mg/m^2, intravenously every 2 weeks. Patients were accrued in a 3+3 design. The study included a preliminary assessment after the first 13 evaluable patients. The trial would be terminated early if 0 or 1 responses were observed in these patients.
RESULTS: Twelve patients were treated over 2 dose levels (nal-IRI 50 and 70 mg/m^2). At dose level 2, nal-IRI 70 mg/m^2, 2 of 3 patients developed dose-limiting toxicities including 1 patient who developed grade 4 neutropenia and grade 3 diarrhea and anorexia and 1 patient with grade 3 diarrhea, hypokalemia fatigue, and anorexia. Accrual to dose level 1 was expanded to 9 patients. The Drug Safety Monitoring Board (DSMB) reviewed the data of the initial 12 patients-there were 0/12 responses (0%) and the median progression-free survival was 2 months and accrual was halted.
CONCLUSIONS: The maximum tolerated dose of nal-IRI was 50 mg/m^2 every 2 weeks with TMZ 50 mg/m^2/d. The dose-limiting toxicities were diarrhea and neutropenia. No activity was seen at interim analysis and the study was terminated.

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