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Phase 1 and expanded imaging study of tozuleristide in patients with pediatric primary central nervous system tumors

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Abstract

Objective: Fluorescence-guided surgery has been shown to increase the extent of resection in adult high-grade glioma. The peptide-dye conjugate tozuleristide is a fluorescence-guided surgical agent under development to aid in visualization of tumor tissue during CNS tumor resection. The goals of this study were to assess safety, pharmacokinetics, and the fluorescent signal of tozuleristide in primary CNS tumors in pediatric patients with CNS cancers and to determine a recommended dose for phase 2 studies.

Methods: Tozuleristide was administered intravenously before surgery. Doses from 1.7 mg/m2 to 17.3 mg/m2 were assessed in the dose-escalation part of the study (n = 15). Safety, pharmacokinetics, and imaging data were collected in these patients and in the dose expansion cohort receiving 15 mg/m2 tozuleristide (n = 17).

Results: Twenty-nine patients were enrolled and received tozuleristide, 3 of whom were re-enrolled and re-treated before a second surgery (32 cases total). There were no dose-limiting toxicities, no evidence of allergic reactions, no early withdrawals from the study, and no deaths within 30 days of treatment. In 23 cases, patients received 13.9-17.3 mg/m2 tozuleristide, and the mean ex vivo tumor fluorescence intensity was approximately fivefold higher in these patients (vs lower doses), supporting 15 mg/m2 as an appropriate dose in this patient population. At these doses, intraoperative in situ tumor fluorescence was observed in the majority of cases (16/23, 69.6%) and in both newly diagnosed and recurrent tumors across a range of tumor histologies and grades. For excised tissue specimens from 28 cases for which ex vivo fluorescence imaging was performed, ad hoc analysis showed 81% sensitivity and 93% positive predictive value.

Conclusions: Tozuleristide was well tolerated. The data suggest that tozuleristide fluorescence may be applicable in a range of pediatric CNS tumors and clinical scenarios, providing a useful adjunct to neurosurgeon experience in distinguishing tumor from nontumor tissue.

Keywords: BLZ-100; cancer; central nervous system; fluorescence-guided surgery; oncology; safety; tozuleristide; tumor.