Phase 1 Study of Superselective Intraarterial Cerebral Infusion of Temozolamide after Osmotic Blood/Brain Barrier Disruption for Malignant Glioma

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Introduction

Temozolamide is part of the standard treatment of malignant glioma, however, data suggests it may not effectively penetrate the blood/brain barrier (BBB). This phase I trial sought to assess the safety and to determine the maximum tolerated dose of superselective intraarterial cerebral infusion (SIACI) of Temozolamide after osmotic disruption of the BBB with mannitol in patients with recurrent malignant glioma.

Methods

A total of 21 patients with recurrent malignant glioma were included in the current study. The starting dose of temozolamide was 75 mg/m2 and dose escalation was done to 250 mg/m2. All patients were observed for 28 days post-infusion for any side effects. Adverse events were noted per the Common Terminology Criteria for Adverse Events (CTCAE) v4.2.

Results

There was no dose-limiting toxicity from a single dose of SIACI of temozolamide up to 250 mg/m2 after osmotic BBB disruption with mannitol. There were two adverse events, both at the 100 mg/m2 dosage. One patient had left hemiparesis immediately following the IA procedure, which was a grade 3 AE. Another patient had worsening of pre-existing neurological symptoms, a grade 2 AE. There were no other significant adverse events.

Conclusions

SIACI of mannitol followed by temozolamide (up to 250 mg/m2) for recurrent malignant glioma is well tolerated. A Phase II trial is currently underway to determine both safety and efficacy of SIACI of temozolamide with chemo-radiation in patients with newly diagnosed high-grade glioma.

Learning Objectives

By the conclusion of this session, participants should be able to 1) Discribe the importance of enhancing chemotherapy delivery to malignant gliomas, 2) Discuss, in small groups the utility of superselective intra-arterial drug delivery for brain tumors, 3) Identify a potentially effective treatment modality of malignant gliomas

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