JOURNAL ARTICLE

CTNI-57. PRELIMINARY RESULTS OF A PHASE 1 TRIAL OF ORAL GALLIUM MALTOLATE IN RECURRENT GLIOBLASTOMA

Jennifer Connelly, Casey Zoss, Kathleen Schmainda, Mona Al-Gizawiy, Fernando Santos Pinheiro, Christopher Chitambar

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Abstract

BACKGROUND

Glioblastoma (GBM) is an aggressive brain tumor with a dismal prognosis. New drugs that exploit previously underexplored cancer-related pathways are needed. We and others have shown that GBM stem cells require significantly greater amounts of iron than normal cells to drive critical iron-dependent processes that are altered in malignancy. We showed that oral gallium maltolate (GaM), an iron-targeting metal compound, has significant activity against GBM stem cells in vitro and shrinks GBM tumors and prolongs survival in a rat brain tumor model. GaM's mechanisms include inhibition of cellular iron homeostasis, ribonucleotide reductase, and mitochondrial complex 1. Further study of GaM's toxicity and benefit in patients with recurrent GBM is warranted.

METHODS

The Phase 1 trial design follows a 3 + 3 dose escalation scheme. Eligible patients will receive GaM at 3 dose levels: 500, 1,000, or 1,500 mg/day for a minimum of two 28-day cycles. Hepatic, renal, and hematologic functions, iron panel, and gallium levels are monitored every 2 weeks. Toxicity and tumor response are assessed by NCI CTCAE criteria and by RANO criteria, respectively. Patients with responding or stable disease may continue treatment with monitoring.

RESULTS

Ten patients have completed treatment at dose levels 1 and 2 and eight patients are evaluable. Four patients enrolled after first recurrence while the other four patients enrolled after their second, third (2 patients) and fourth recurrence. Median progression-free survival (PFS) on treatment was 118 days. Three patients experienced PFS >180 days and two of those patients remain on treatment. To-date, no dose-limiting toxicities (DLTs) at dose levels 1 and 2 have been encountered.

CONCLUSIONS

Oral GaM is well tolerated without significant DLTs to date. An additional 6 patients are presently enrolled at dose-level 3. Updated toxicity data and clinical outcomes of the study will be presented at the annual SNO meeting.