Intraarterial Chemotherapy for Glioblastoma: Where We Are Now and Where We Are Going?

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Introduction

Intraarterial chemotherapy with blood/brain barrier (BBB) disruption may allow for increased efficacy of treatment for malignant glioma. We present a summary of our clinical trials using this treatment paradigm and highlight our future directions.

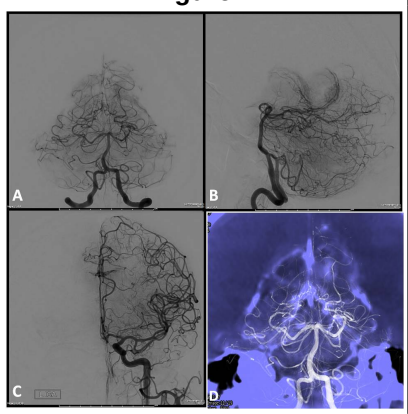
Methods

Phase I/II clinical trials were conducted between 2009-2017 to evaluate the safety and efficacy of selective intraarterial infusion (SIACI) of mannitol for osmotic BBB disruption and infusion of either bevacizumab, cetuximab, or temozolomide into the arterial distribution of high grade gliomas.

Results

A trial using SIACI of bevacizumab after osmotic BBB disruption in 30 patients with recurrent glioblastoma found that it was safe and well tolerated, and could reduce tumor volume. A second trial of 14 GBM patients showed a PFS of 10 months with a single dose of IA bevacizumab. A follow up trial with 16 patients showed that a single dose of SIACI of bevacizumab had a progression-free durability of 4 months. SIACI of cetuximab and temozolomide for glioblastoma were shown to be safe and well tolerated in completed phase -I trials, with temozolomide offering a median survival of 2 years. A trial of 12 pediatric patients with diffuse intrinsic pontine glioma (DIPG) also showed that SIACI of cetuximab and bevacizumab was well-tolerated and offered symptom relief. A subgroup analysis of 65 glioblastoma patients who received SIACI of bevacizumab showed that MRI imaging could be used to predict survival.

Figure 1

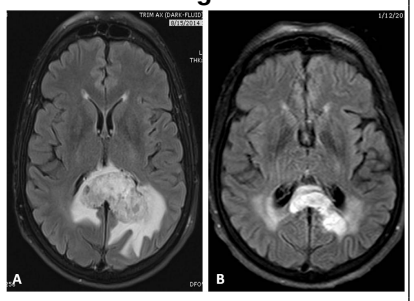


A 60-year old woman with glioblastoma of the splenium underwent selective intraarterial cerebral infusion of mannitol for blood/brain barrier disruption, followed by infusion of bevacizumab. This shows a digital subraction angiogram demonstrating tumor blush, and a 3-dimensional CT angiogram merged with MRI showing the arterial supply to the tumor.

Conclusions

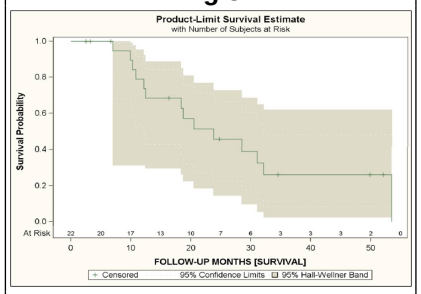
Intraarterial chemotherapy for focal glioblastoma treatment is a promising treatment modality that could improve tumor control and limit systemic toxicity. Over 125 patients have been treated with BBB disruption followed by SIACI of chemotherapy with good safety and results suggesting improved efficacy. Phase II trials are underway to better evaluate efficacy, and as newer BBB disruption techniques such as laser interstial thermal therapy (LITT) or focused ultrasound are developed, this may improve survival for glioblastoma patients.

Fig 2



This shows the reduction in size of the glioblastoma and tumor control 10 months post-procedure.

Fig 3



Kaplan-Meier survival analysis of a Phase I trial of SIACI of mannitol followed by temozolomide for glioblastoma demonstrating median survival of 23.8 months, 95% CI: 12.1 to 32.1 months, mean: 27.8 months, standard error: 4.2.

Learning Objectives

Following this presentation, viewers will better understand the treatment modality of intraarterial chemotherapy, the potential survival benefits, its low side effect profile, and techniques by which to focally target the arterial distribution of the tumor. Future directions of intraarterial chemotherapy trials will be discussed, as will be the use of new modalities being developed to disrupt the blood/brain barrier such as LITT, focused ultrasound, and nanoparticles etc.

References

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