PILOT STUDY OF PHOSPHODIESTERASE-V INHIBITION TO INCREASE INTRATUMORAL CONCENTRATION OF CARBOPLATIN IN PATIENTS WITH RECURRENT HIGH GRADE GLIOMAS AND BRAIN METASTASES (IRB #17009)

Conventional treatment of malignant gliomas consists of surgery, radiotherapy and chemotherapy, which may provide symptom relief and extend survival for a short period of time. Despite standard treatment, recurrences of high grade malignant gliomas are common. Response rates in recurrent glioblastoma multiforme patients are limited with poor progression free survival and overall survival rates.

Currently, there is limited treatment for recurrent high grade malignant gliomas and brain metastases. Improvement in the management of both primary and metastatic tumors will require improved chemotherapeutic approaches to optimize drug delivery across the blood brain barrier.

The blood brain barrier is a protective structure in the central nervous system that restricts certain chemical substances and bacteria from passing between the bloodstream and neural tissue. The blood brain barrier helps maintain a constant environment for the brain, limiting the possibilities of infection in the brain. However, this same protective structure presents a challenge in treating most brain disorders, including tumors, making it difficult to deliver therapeutic agents, like chemotherapy, to the brain. Chemotherapy agents that could be potentially more effective in treating brain tumors are limited by their inability to fully cross the blood brain barrier.

Chemotherapeutic agents, including carboplatin have been used for the treatment of primary malignant gliomas and metastatic brain cancer. It has been shown that carboplatin could be administered safely with an agent that opens the brain tumor barrier for the treatment of primary and/or metastatic brain tumors. Initial studies have shown that the vardenafil had the greatest ability to increase the permeability of the blood brain/tumor barrier.

This study aims to determine the ability of vardenafil to increase the concentration of carboplatin, a systemically delivered chemotherapy, in patients with recurrent malignant gliomas or metastatic brain cancer.

Patients with malignant gliomas who fit eligibility criteria will be seen by their treating physicians in the clinic for standard of care treatment and will be approached and consented for participation prior to surgery. Part of inclusion requirements for patients who have undergone biopsy or previous surgery is standard of care pathology review to confirm diagnosis. Patients will be randomized to one of two arms on this trial: standard of care treatment arm which consists of carboplatin alone or experimental treatment arm of levitra and carboplatin. Patients in the experimental treatment arm will be given levitra 1-2 hours prior to surgery and carboplatin will be administered 30 minutes before the procedure.
Additionally, analysis of the subject's tumor tissue will occur in this trial. This will occur on two occasions. After the subject consents to participation, the pathology report related to the tumor tissue taken during a subject's prior standard of care biopsy will be reviewed to confirm diagnosis (this is standard of care). Then, in regards to the tissue that is gathered during surgery, the left over tissue (after all standard analysis is performed by Pathology) will be analyzed by the study team to determine carboplatin concentration (research related procedure). No extra tissue will be taken for research purposes. Patients will come back 2 weeks post-surgery and treatment for standard of care visit where they will have standard of care laboratory blood tests. The study team will record the analysis of these blood tests for research. No additional blood will be drawn for research purposes. 4 weeks post-surgery and treatment patients will return for another standard of care visit where laboratory blood will be collected and neurological evaluation will be done for standard of care. The only research procedures that will occur during follow-up will be urine tests and a pregnancy test (if applicable). Patients will be in the study an estimated 4 weeks.

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