

The Safety and Efficacy of DCA for the Treatment of Brain Cancer

This study has been completed.

First Received: October 4, 2007 Last Updated: February 5, 2010 [History of Changes](#)

Sponsor:	University of Alberta
Collaborator:	Capital Health, Canada
Information provided by:	University of Alberta
ClinicalTrials.gov Identifier:	NCT00540176

Purpose

Malignant gliomas, which include Glioblastoma multiforme (GBM), are the most common and most aggressive types of brain cancer, accounting for approximately 60% of primary brain tumors. These tumors are characterized by diverse molecular abnormalities (within the same tumor), which, along with the difficulties of many standard chemotherapies crossing the blood barrier, contribute to the very poor response to therapy and poor survival.

We recently showed that Dichloroacetate (DCA, an inhibitor of the mitochondrial pyruvate dehydrogenase kinase) was able to depolarize cancer (but not normal) mitochondria and induce apoptosis in cancer but not normal tissues. We believe that altering the metabolism of cancers like glioblastoma (DCA switches metabolism from the cytoplasmic glycolysis to the mitochondrial glucose oxidation) we inhibit the resistance to apoptosis that characterizes cancer. Because metabolism (i.e. glycolysis) is the end result of many and diverse molecular pathways, the effects of DCA might be positive in cancers with diverse molecular backgrounds. DCA is also a very small molecule that readily crosses the blood brain barrier. Therefore we hypothesize that DCA will be an effective and relative non-toxic potential therapy for malignant gliomas.

We are conducting a phase II trial with 2 parallel arms: a) patients with newly diagnosed malignant gliomas and b) patients with recurrent gliomas or gliomas that have failed standard therapy (which includes surgery, radiotherapy and chemotherapy). All patients need to have a histological diagnosis. DCA will be given orally and patients will be followed for a minimum of 6 months. The tumor size will be followed by standard MRI or CT criteria and glucose uptake (a direct effect of DCA on the tumor) will be measured by FDG-PET imaging. Several clinical parameters and quality of life will be followed. Potential toxicity (particularly peripheral neuropathy) will be closely followed and dose-de-escalation protocols are in place in case of toxicity. In addition, escape protocols for the application of standard therapy (when appropriate) are in place in patients with no evidence of response to DCA. In vitro studies will be performed in the tissues obtained at the time of surgery (where appropriate) and correlated prospectively with clinical data.

There is limited ability to accept patients outside of Alberta; this is in part because the visit and testing schedule is intense, requiring residence in Edmonton for at least 6 months.

Condition	Intervention	Phase
Malignant Gliomas, Glioblastoma Multiforme	Drug: Dichloroacetate (DCA)	Phase II

Study Type: Interventional
Study Design: Endpoint Classification: Safety/Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Treatment

Official Title: A Phase II Open-labeled, Double-arm Clinical Study of Dichloroacetate (DCA) in Malignant Gliomas and Glioblastoma Multiforme (GBM) Patients

Resource links provided by NLM:

[MedlinePlus](#) related topics: [Brain Cancer](#) [Cancer](#) [Surgery](#)

[Drug Information](#) available for: [Dichloroacetate](#) [Sodium dichloroacetate](#)

[U.S. FDA Resources](#)

Further study details as provided by University of Alberta:

Primary Outcome Measures:

- To determine the therapeutic response to oral Dichloroacetate (DCA) in patients with malignant gliomas, utilizing standard criteria for the objective response of tumor size to treatment (CT and/or MRI).
- To evaluate the safety and tolerability of oral (DCA) in patients with gliomas.
- To determine the progression-free survival (PFS) and overall survival achieved with oral DCA in patients with gliomas.

Secondary Outcome Measures:

- To evaluate the in vitro effects of DCA on cell proliferation/apoptosis and mitochondrial function in malignant glioma tissues taken from enrolled patients at the time of surgery and correlate them with clinical data.
- To evaluate glucose uptake using 18F-FDG Positron Emission Tomography (PET) scanning as a biological marker for predicting subsequent therapeutic response to oral DCA in patients with malignant gliomas.

Estimated Enrollment: 50
Study Start Date: October 2007
Study Completion Date: August 2009

Arms	Assigned Interventions
Cohort A: Experimental Recurrent disease with previous surgery, radiation therapy and/or chemotherapy	Drug: Dichloroacetate (DCA) Oral DCA given twice daily for the 24 week period of the study. Continuation of therapy will be indefinite if efficacious.
Cohort B: Experimental Newly diagnosed disease with no previous therapy	Drug: Dichloroacetate (DCA) Oral DCA given twice daily for the 24 week period of the study. Continuation of therapy will be indefinite if efficacious.