

# Bevacizumab does not extend lives of newly diagnosed glioblastoma patients

March 6 2014, by Nancy Fredricks

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(Medical Xpress)—Results from a randomized, phase 3 clinical trial conducted by the Radiation Therapy Oncology Group (RTOG) have shown that adding bevacizumab, a drug that inhibits the growth of blood vessels, to the treatment of glioblastoma (GBM) does not improve patient survival.

Results appear in the Feb. 20, 2014, issue of the *New England Journal of Medicine*. Arnab Chakravarti, MD, chair of [radiation oncology](#) at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital & Richard J. Solove Research Institute (OSUCCC – James) served as national translational research study chair of the international RTOG study. Mark Gilbert, MD, a professor of neuro-oncology with the University of Texas MD Anderson Cancer Center, served as the clinical principal investigator of the overall study.

GBM is the most common form of adult brain cancer. It has an average survival of less than 16 months, and few patients live beyond five years. The growth of new [blood vessels](#) is a characteristic of GBM development, and this growth is stimulated by a substance released by GBM cells called vascular endothelial growth factor A (VEGF-A).

Bevacizumab is an antibody-based drug that targets VEGF-A to block the growth of tumor-derived blood vessels. Clinical trials evaluating the addition of bevacizumab to standard treatment for recurrent GBM demonstrated clinical benefit and led to the drug's Food and Drug Administration [approval](#) in 2009 as a second-line therapy for GBM as a

single agent.

In this new study, researchers sought to determine if administering bevacizumab as part of first-line treatment improved survival among GBM patients. An unprecedented 621 adult study participants were enrolled to the multicenter trial and randomized into one of two study arms, with treating physicians blinded to treatment assignment. All participants consented to provide tumor tissue and blood samples for future research as part of the study.

Study participants were assigned equally across study arms using DNA-methylation status as a predictor of patient response to therapy. Previous studies have suggested that patients with methylated tumor promoters do significantly better than those with unmethylated tumor promoters. Because of this, researchers hypothesized that patients with a worse prognosis—as determined by their tumor marker—would do better if they received bevacizumab as a first-line treatment.

All participants were given standard-of-care consisting of radiation therapy and daily temozolomide chemotherapy. Starting at week four of [radiation therapy](#) and continuing every two weeks until disease progression, several treatment-related toxicities occurred or completion of adjuvant chemotherapy, patients randomized to the experimental arm of the study received bevacizumab while the control group received a placebo.

Study design allowed researchers to compare risk and benefit of early versus late treatment. Authors report a median survival of 20.5 months, which revealed no statistical difference in overall survival between the two study arms and suggested no added benefit to giving bevacizumab as a first-line therapy in terms of survival.

"The results of this trial demonstrate that personalized care approaches

are desperately needed for glioblastoma (GBM) patients and that a 'one glove fits all approach' may be less fruitful in the management of GBMs," says Chakravarti, principal investigator of the local arm of study, which enrolled about 10 patients to the study.

"Through careful molecular, genetic and epigenetic profiling, our teams within the RTOG and the Ohio State University Comprehensive Cancer Center are uncovering the underlying mechanisms that contribute to treatment resistance in these most devastating tumors," adds Chakravarti. "What we are beginning to understand is that GBMs are comprised of dozens—if not hundreds—of distinct molecular subtypes of tumors. Novel therapies such as [bevacizumab](#) must be personalized towards an individual's tumor versus being directed towards a broad histopathological class of tumors so that the appropriate patient population may benefit."

Provided by Ohio State University Medical Center

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