Study finds glioblastoma patients treated with bevacizumab experience reduced cognitive function and quality of life

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Many glioblastoma patients treated with bevacizumab (Avastin) have significant deterioration in neurocognitive function, symptoms and quality of life. Not only that, the changes often predict treatment outcomes, according to new research from The University of Texas MD Anderson Cancer Center.

The findings from the large national multi-center Phase III trial, RTOG 0825, were presented today at the annual meeting of the American Society of Clinical Oncology.

Glioblastoma is the most frequent and aggressive type of brain tumor. Despite slight gains, tumors pose a high risk of recurrence and are commonly fatal.

Previous studies found bevacizumab, a monoclonal antibody directed against the vascular endothelial growth factor, prolongs progression-free survival (PFS) in patients with recurrent glioblastoma.

RTOG 0825, one of the largest trials to study the clinical benefit of a brain tumor treatment, evaluated newly diagnosed patients treated with bevacizumab, in addition to standard chemoradiation and maintenance temozolomide, versus those who received a placebo and standard treatment.

Tests measured effects of treatment

Using objective tests of cognitive function and subjective measures of symptoms and quality of life, 507 patients were evaluated at diagnosis and at intervals throughout treatment as long as scans showed their tumors were not progressing.

"Most studies rely on traditional endpoints, including overall survival and radiographic outcomes, such as PFS, with little attention to the impact of the disease and therapies on the patient," said Jeffrey Wefel, Ph.D., associate professor in MD Anderson's Department of Neuro-Oncology and a senior author on the study. "This makes the potential clinical benefit difficult to ascertain."

Neurocognitive changes

At the beginning of the study, patients' neurocognitive function in both groups was below healthy population norms. Longitudinal analyses showed those treated with bevacizumab compared to ones treated with placebo demonstrated greater decline in global neurocognitive function, executive function (skills involved in tasks such as planning, organizing and multi-tasking) and processing speed.

Additionally, baseline performance and early change (through week 10) in global neurocognitive function, memory, executive function and processing speed were prognostic for survival.

"Relatively little attention has been directed toward investigating patient biomarkers associated with outcomes," Wefel said. "We sought to determine if patient cognitive function was a biomarker associated with progression-free and overall survival (OS) time. We found patients with worse cognitive function at baseline, and those who experienced

cognitive decline after concurrent chemoradiation with or without bevacizumab, were at greater risk for shorter PFS and OS time."

Quality of life and side effects

Symptoms and quality of life were significantly worse for patients receiving bevacizumab, particularly at weeks 22 and 34. In particular, symptom burden, including treatments, and generalized and affective symptoms were greater, with persistent differences seen in treatment-associated symptoms. Additionally, overall symptom burden, tumor and treatment-related symptoms, as well symptoms that interfered with daily activities, were also worse for those on bevacizumab over the treatment course.

Baseline and early change rating of both symptoms and quality of life, like neurocognitive function, were also prognostic for survival.

"The idea of our research was to put together the total picture of this treatment, not only how it affects the tumor, but how it affects patients and how they go about their lives," said Terri Armstrong, Ph.D., adjunct professor in MD Anderson's Department of Neuro-Oncology. "It was our hope this treatment would improve life for them, but that just wasn't the case. For many, both tumor and treatment-related symptoms were worse and continued to get worse over time."

Next steps

"We're eager to continue investigating the data within this trial to identify subsets of patients for whom a particular therapeutic approach may have been associated with a favorable net clinical benefit for survival, cognition, symptoms and quality of life," Wefel said.