Biomarkers predict brain tumor's response to therapy

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A report in *Cancer Research*, a journal of the American Association for Cancer Research, highlights a new biomarker that may be useful in identifying patients with recurrent glioblastoma, or brain tumors, who would respond better to anti-vascular endothelial growth factor therapy, specifically cediranib.

Cediranib is a highly potent inhibitor of vascular endothelial growth factor (VEGF) receptor tyrosine kinases. It is an investigational, oral agent that is administered once daily. Using a form of magnetic resonance imaging (MRI) that looked at the mechanism of action of this agent, the researchers were able to determine, even as early as after a single dose of cediranib, those patients who benefited from the agent and those who did not.

"We found that results from an advanced MRI scan taken just a day after starting treatment correlated with survival. Combining MRI with blood biomarkers did an even better job of identifying patients who best responded to treatment," said researcher A. Gregory Sorensen, M.D., associate professor of radiology and health sciences and technology at Harvard Medical School, Massachusetts General Hospital. "If this approach is validated in larger studies, we could use these tools to keep patients on therapies that their tumors respond to, and shift non-responders to other therapies much earlier."

Sorensen and colleagues sought to find the potential biomarkers that could be used to predict those patients who would respond better from

antiangiogenic therapy early in the course of treatment by use of MRI.

The researchers measured vascular normalization prior to and one day after patients' received cediranib using an advanced MRI technique. They performed blood analysis and examined correlations between vascular parameters and treatment response after a single dose of cediranib in 31 patients with recurrent glioblastoma; all biomarkers were measured in 28 patients.

"Vascular normalization is an important mechanism of how these drugs work in cancer patients," said Rakesh K. Jain, Ph.D., Andrew Werk Cook professor of tumor biology at Harvard Medical School and director of the Edwin L. Steele Laboratory for Tumor Biology in the department of radiation oncology at Massachusetts General Hospital Cancer Center, Boston. Jain is also a researcher on this study.

The correlative analysis in this single arm, phase II study showed that those patients whose extent of vascular normalization was greater, had a longer duration of overall survival as well as progression-free survival, according to Jain. Median overall survival rate was 227 days; some patients lived for about two years and some lived less than two months.

"I was intrigued by the findings from this innovative trial, especially the fact that you could use separate biomarkers in combination to potentially predict the outcomes of patients," said Richard B. Gaynor, M.D., Ph.D., deputy editor of Cancer Research. Gaynor is the vice-president of cancer research at Eli Lilly and Company.

"This is really a severe disease and being able to determine response at such an early point is helpful to tailor treatment," he said. "If we can predict those responding to antiangiogenic therapy early on, we may be able to define where the benefit would be."

These findings need to be validated in larger, prospective studies. The researchers are currently conducting several studies based on these promising results in efforts to evaluate the benefits and prolonged survival of these patients.

One study is a phase III, randomized, multicenter, international trial that will compare patients treated with standard chemotherapy, those treated with cediranib, and those treated with a combination of the two to evaluate the effects and prolongation of life in all three cohorts. Approximately 300 patients are enrolled in this study, with enrollment halfway complete, according to Jain.

Another study, which just began enrollment, is a phase II, single-arm trial among patients who are newly diagnosed with glioblastoma. Researchers plan to evaluate treatment effects in patients treated with this agent combined with standard radiation and chemotherapy.

"We hope to develop biomarkers to help physicians and researchers know if a patient is responding; if they are not responding we can move them to a more effective therapy, if they are responding we can continue treatment, even if the treatment carries risks or side effects," Sorensen said.

Source: American Association for Cancer Research (news : web)