DNA-level biomarker can predict overall survival for rare brain tumors

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MGMT promoter methylation status—information gathered at a DNA-level—can help predict overall survival for patients with a rare form of brain cancer known as anaplastic astrocytoma, according to a new analysis from The Ohio State University Comprehensive Cancer Center - Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC - James).

The goal of this study was to determine the number of patients with positive MGMT promoter methylation status and its significance as a means of predicting survival outcomes for patients with anaplastic astrocytomas. Erica Bell, PhD, assistant professor of radiation oncology served as first author of the study. Arnab Chakravarti, MD, chair of radiation oncology at the OSUCCC - James, was senior author and principal investigator.

MGMT is a noted DNA repair gene and known biomarker in grade 4 glioblastoma brain tumors, however, data on its prognostic value in other grade 2 and grade 3 forms of brain tumors has been unclear. MGMT promoter methylation was calculated using the MGMT-STP27 model in this study.

"The medical community has suspected that MGMT status could be used as a biomarker for predicting overall survival in these patients, but access to a large set of well-controlled clinical data and matched specimens to confirm this was lacking," says Bell. "Our study represents the first data confirming that MGMT promoter methylation status can be

used as an independent biomarker for predicting overall survival in grade 3 tumors."

She notes that this knowledge will help oncologists identify patients less likely to respond to treatment based on the biology of their tumors and design better clinical trials.

Bell will present the findings (Abstract No. 2781) on Sept. 26, 2017, at the annual meeting of the American Society for Radiation Oncology (ASTRO) in San Francisco, where she will also receive one of the 2017 "Best of ASTRO" awards.

Study Design and Results

For this study, researchers analyzed data from a national cooperative group trial (RTOG 9813) that enrolled 196 high-risk patients with anaplastic astrocytoma. Patients were randomized into one of two treatment arms: radiation therapy plus nitrosourea or radiation therapy and temozolomide.

MGMT promoter methylation status was calculated for 58 patients - 62 percent of patients tested positive for the biomarker. Bell and colleagues then specifically analyzed MGMT promoter methylation in correlation with overall and progression-free survival outcomes. Patients who had the MGMT biomarker also had higher overall survival compared with patients whose tumors did not carry this biomarker. No significant difference in progression-free survival was observed, although there was a trend toward significance.

Bell says the next step is to develop better predictive biomarker models that incorporate all known markers, not just MGMT.

"This will help us better understand which specific patients are not doing

well on standard-of-care and enroll those patients to clinical trials that will give us the best chance of cancer control," she adds. "If we understand which patients aren't doing well on standard of care, we can really focus on designing specific clinical trials to help those patients achieve better overall survival."

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