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Genetic Biomarker Linked to Improved Survival for Patients With Certain Brain Tumors

COLUMBUS, Ohio – A DNA-level biomarker (*MGMT* promoter methylation) can be used to help predict survival outcomes in patients with high-risk, low-grade gliomas, according to a new study conducted through the NRG Oncology/RTOG collaborative clinical trials group and led by scientists at The Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC – James).

New data reported in the June 28, 2018, issue of the medical journal *JAMA Oncology* shows that patients with *MGMT* methylated tumors are more than twice as likely to survive after combination temozolomide and radiation treatment than patients with unmethylated tumors.

Gliomas are a class of brain tumors that develop in the supportive cells that surround nerve cells in the brain.

Study Methods and Results
Previously reported findings from the NRG Oncology/RTOG 0424 clinical trial report a three-year overall survival benefit for certain brain tumor patients who receive the drug temozolomide in addition to radiation therapy compared with the standard of care. Data regarding the significance of *MGMT* promoter methylation status, however, was not examined.

This new study represents the first published data showing that *MGMT* promoter methylation status can be used to predict patient outcomes.

Researchers conducted a retrospective analysis of 129 glioma patients who participated in the NRG Oncology/RTOG 0424 clinical trial. Of these patients, 75 patients had tissue samples available that could be analyzed for *MGMT* promoter methylation status.

Using various statistical methods, researchers confirmed that *MGMT* promoter methylation can be used as an independent prognostic biomarker of high-risk, low-grade glioma in patients treated with temozolomide and radiotherapy.

“Identifying biomarkers – prognostic and predictive markers – is critical for personalizing care and giving patients the best quality of life and chances of longer survival,” says Arnab Chakravarti, MD, senior author of the study and chair of radiation oncology at the OSUCCC – James. “These tumors are tricky to treat because there is such a wide range of outcomes. Some patients succumb to the disease within months, others live years beyond their diagnosis. We need better methods of determining which patients are likely to have more aggressive tumors.”

This new data represents the first clinical trial-based evidence of the prognostic importance of *MGMT* promoter methylation in patients with grade II glioma. Previously published data on *MGMT* promoter methylation as a biomarker of survival outcomes is related to the malignant brain tumor, glioblastoma.

"This is also the first data to highlight the test's potential prognostic value beyond a standard molecular test currently used (*IDH1/2* mutation status) to help predict patient survival outcomes," adds Erica Bell, PhD, first author of the study and scientist with the OSUCCC – James Translational Therapeutics Research Program.

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Collaborators come from the OSUCCC – James, NRG Oncology, London Regional Cancer Program, Wake Forest University, Toronto General Hospital/Princess Margaret, St. Joseph's Hospital and Medical Center-Accruals Arizona Oncology Services Foundation, Thomas Jefferson University Hospital, Henry Ford Hospital, Hospitalier de L ' Universite de Montreal-Notre Dame,University of Maryland Medical Systems, H. Lee Moffit Cancer & Research Institute, Mayo Clinic, University of Washington Medical Center-Accruals, University of California-San Francisco, University of Wisconsin Hospital-Madison, and Baptist Hopsital of Miami and include: Peixin Zhang, PHD, Barbara Fisher, MD, David Macdonald, MD, Joseph McElroy, PhD, Glenn Lesser, MD, Jessica Fleming, MD, Arup Chakraborty, PhD, Ziyann Liu, Aline Becker, MD, PhD, Denise Fabian, MD, Kenneth Aldape, MD, Lynn Ashby, MD, Maria Werner-Wasik, MD, Eleanor Walker, MD, Jean-Paul Bahary, MD, Young Kwok, MD, Michael Yu, MD, Nadia Laack, MD, Christopher Schultz, MD, Heidi Gray, MD, Ian Robins, MD, PhD, and Minesh Mehta, MD.

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