Secondary Analysis of NRG-RTOG 0525 Develops Validated Molecularly-Based Classification Model for Glioblastoma

PHILADELPHIA, PA — NRG Oncology researchers have developed an improved model to predict glioblastoma patients’ response to radiation temozolomide chemotherapy. A secondary analysis of the clinical trial NRG-RTOG 0525 Radiation Therapy (RT) and Temozolomide (TMZ) in Treating Patients with Newly Diagnosed Glioblastoma or Gliosarcoma was initiated to refine the existing, clinically-based partitioning analysis (RPA) model by incorporating molecular variables. The results of this analysis were published in the Journal of the American Medical Association (JAMA) Oncology on January 12, 2017.

“This new model, which was biologically validated, improves outcome stratification for patients with glioblastoma that are treated with radiation and temozolomide, and has the potential to contribute to improving the accuracy in assessing prognostic groups for these patients,” says Erica H. Bell, PhD, lead author of the correlative analysis and an Assistant Professor in the Department of Radiation Oncology at The Ohio State University Comprehensive Cancer Center-Arthur G. James Cancer Hospital.

The initial, randomized phase III clinical trial NRG-RTOG 0525 sought to compare two different schedules of temozolomide to determine which was more effective when combined with radiation therapy for patients with newly diagnosed glioblastoma or gliosarcoma. The secondary analysis examined 22 proteins by quantitative immunohistochemistry using specimens from NRG-RTOG 0525 (n=452) to assess the prognostic significance of overall survival.

Protein biomarkers MGMT (HR= 1.81, 95% CI(1.37, 2.39), p<0.001), survivin (HR=1.36, 95% CI(1.04, 1.76), p=0.02), c-Met (HR=1.53, 95% CI(1.06, 2.23), p=0.02), pmTOR (HR=0.76, 95% CI(0.60, 0.97), p=0.03), and Ki-67 (HR= 1.40, 95% CI(1.10, 1.78), p=0.007), were found to be significant upon a single-marker multivariate analysis of overall survival. The protein biomarkers were combined with clinical variables such as age, performance status, extent of resection, and neurological function and were considered for the new RPA model (NRG-GBM-RPA) which comprised of c-Met protein, MGMT protein, and age. The prognostic significance of the NRG-GBM-RPA was subsequently confirmed in an independent dataset.

“Incorporating c-Met and MGMT protein data into the new model helps to enhance the prognostic clarification of patients with glioblastoma, provides further insight into resistance to radiation and temozolomide and potentially guides clinical decision-making in certain cases,” stated Arnab Chakravarti, MD, the corresponding author of the secondary analysis and Chair of Radiation Oncology at The Ohio State University Comprehensive Cancer Center -Arthur G. James Cancer Hospital.

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Molecular-Based Recursive Partitioning Analysis Model for Glioblastoma in the Temozolomide Era: A Correlative Analysis Based on NRG Oncology RTOG 0525
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Erica H. Bell, PhD1 Stephanie Pugh, PhD2 Joseph P. McElroy, PhD1 Mark R. Gilbert, MD3 Minesh Mehta, MD4 Alex Klimowicz, PhD5 Anthony Magliocco, MD6 Markus Bredel, MD, PhD7 Pierre Robe, MD, PhD8 Anca Grosu, MD9 Roger Stupp, MD10 Walter Curran, Jr., MD11 Aline Becker, MD1 Andrea L. Salvaggione, MD1 Jill Barnholtz-Sloan, PhD12 Kenneth D. Aldape, MD13 Deborah T. Blumenthal, MD14 Paul Brown, MD13 Jon Glass, MD15 Luis Souhami, MD, FASTRO16 R. Jeffrey Lee, MD17 David Brachman, MD18 John C. Flickinger, MD19 Minhee Won, MA2 Arnab Chakravarti, MD1

1Ohio State University Comprehensive Cancer Center – Arthur G. James Cancer Hospital 2NRG Oncology Statistics and Data Management Center 3National Institutes of Health 4University of Maryland Medical Systems 5University of Calgary 6Moffitt Cancer Center 7University of Alabama 8Utrecht Cancer Center 9University of Freiburg 10University Hospital Zurich 11Emory University 12Case Comprehensive Cancer Center 13MD Anderson Cancer Center 14Tel Aviv Sourasky Medical Center 15Thomas Jefferson University Hospital 16McGill University Health Centre 17Intermountain Medical Center 18Arizona Oncology Services Foundation 19UPMC-Shadyside Hospital

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