IDH and CIC Mutations Provide Prognostic Information for Grade II and III Gliomas

BOSTON, MA - NRG Oncology investigators have identified two biomarkers that are prognostic of overall and progression-free survival for patients with lower-grade gliomas. This combined mutational analysis using specimens from two NRG Oncology clinical trials is the first study to examine the prognostic effects of mutations within IDH1/2, ATRX, CIC, FUBP1 and the TERT promoter using rigorous multivariate analysis (MVA) in a combined cohort of grade II and grade III gliomas with prospectively-collected, well-annotated clinical data. These results were presented at the American Society of Radiation Oncology (ASTRO) Annual Meeting in Boston, Massachusetts, September 27, 2016.

“The correlative study associated with RTOG 9802 and RTOG 9813 represents the very first to demonstrate independent prognostic value of IDH mutations in a combined cohort of Grade II/III gliomas in the context of well-annotated Phase III clinical studies, thereby extending the findings of TCGA and previously-reported single institution studies. In the present study, IDH gene mutations were found to be of independent prognostic value after age, treatment, extent of surgical resection, histology, and performance status were factored in. Future directions involve investigation of the predictive value of IDH and other biomarkers to guide specific therapeutic selection for Grade II/III glioma patients, which remains highly controversial in this context,” says Arnab Chakravarti, MD of the Ohio State University Comprehensive Cancer Center and Richard L. Solove Research Institute and the Senior Author of RTOG 9802 and 9813.

The analysis utilized a combined cohort of two prospective phase III studies’ (NRG Oncology RTOG 9802 and 9813) specimens from 115 grade II and 104 grade III (n=104) glioma patients. The investigators determined IDH mutation status by immunohistochemistry and/or deep sequencing and used a custom Ion AmpliSeq DNA panel for mutation analysis. Sanger Sequencing was used to detect TERT promoter mutations. The Kaplan-Meier method was used for the analyses on overall survival (OS) and progression-free survival (PFS). Hazard ratios (HRs) on the effect of biomarkers were calculated using the Cox proportional hazard model and tested using the Wald and log-rank tests. MVAs were performed incorporating age, treatment, surgery, histology, and performance status as covariates. Marker by treatment interaction effects were tested using the combined cohort for each marker using the analysis of deviance tests.

Mutations were found within IDH1/2 in 65%, ATRX in 34 percent, TERT promoter in 32%, CIC in 18 percent, and FUBP1 in 6% of the respective analyzed cases. In the univariate analysis, IDH1/2 mutations (OS: HR=0.38; p<0.001; PFS: HR=0.45; p=0.001) and CIC (OS: HR=0.48; p=0.04; PFS: HR=0.50; p=0.04) mutations were significantly associated with better OS and PFS. Upon MVA, IDH1/2 mutations were significantly associated with better OS and PFS (OS: HR=0.50; p=0.001; PFS: HR=0.52; p<0.001), whereas CIC mutations trended toward better OS and PFS (OS: HR=0.47; p=0.073; PFS: HR=0.48; p=0.059). This study defines the prognostic value of IDH mutations
independent of age, treatment, surgery, histology, and performance status, while also providing
evidence of the prognostic value of CIC independent of grade/histology. Tests of these markers to
aid in treatment choice (marker by treatment interaction effects) did not reach statistical significance;
however, efforts to increase sample size are ongoing.

NRG Oncology RTOG 9802 and 9813 were funded by grants from the National Cancer Institute,
Merck & Co., the Brain Tumor Funders Collaborative Grant, and the Ohio State University CCC.

Full Citation
A Mutation Prognostic Biomarker Study in Grade II and Grade III Gliomas Utilizing a Combined Cohort of NRG
Oncology/RTOG 9802 and 9813.
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patients with cancer. Founded in 2012, NRG Oncology is a Pennsylvania-based nonprofit corporation that integrates the
research of the National Adjuvant Breast and Bowel Project, the Radiation Therapy Oncology Group, and the Gynecologic
Oncology Group. The research organization seeks to carry out clinical trials with emphases on gender-specific
malignancies, including gynecologic, breast, and prostate cancers, and on localized or locally advanced cancers of all
types. NRG Oncology’s extensive research organization comprises multidisciplinary investigators, including medical
oncologists, radiation oncologists, surgeons, physicists, pathologists, and statisticians, and encompasses more than 1300
research sites located world-wide with predominance in the United States and Canada. NRG Oncology is supported
primarily through grants from the National Cancer Institute (NCI) and is one of five research groups in the NCI’s National
Clinical Trials Network.