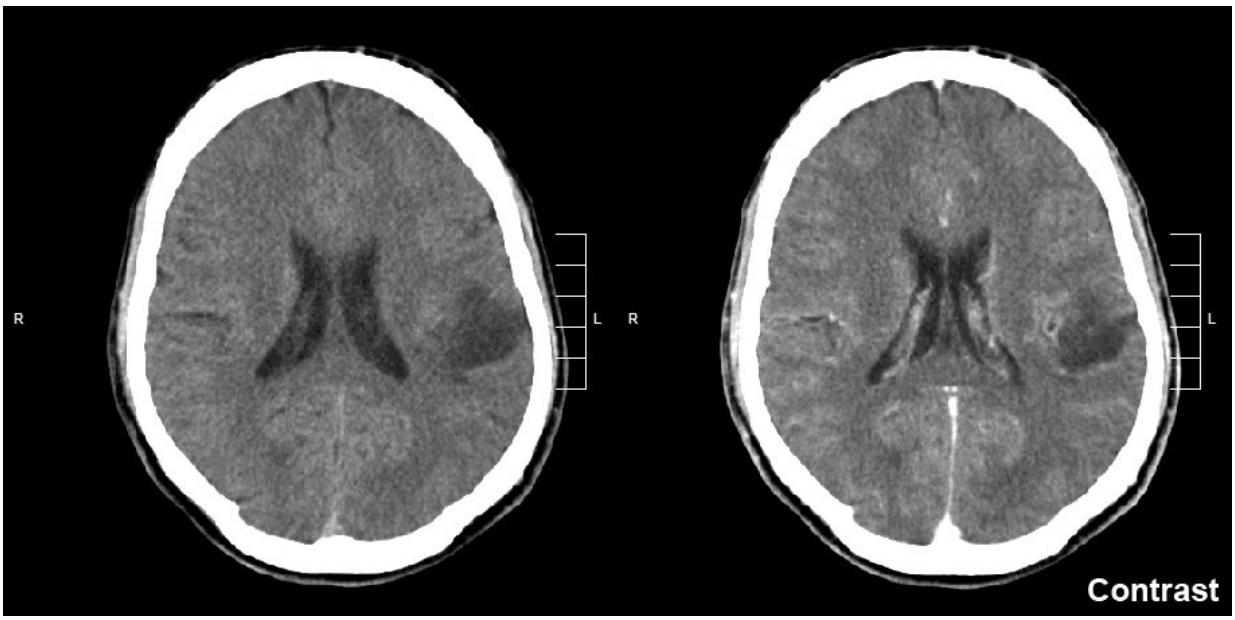
Genomic analysis predicts survival benefit of adjuvant chemotherapy following radiotherapy

August 31 2020



Glioma of the left parietal lobe. CT scan with contrast enhancement. Credit: Mikhail Kalinin/CC BY-SA 3.0

A practice-changing study, NRG Oncology clinical trial NRG-RTOG 9802, has demonstrated, for the first time, a survival benefit of adjuvant chemotherapy following radiotherapy over radiotherapy alone in certain subgroups of patients with high-risk, low-grade glioma (WHO classification: LGG, grade II), a type of brain tumor that originates from

glial cells.

The study results, published in a recent issue of the *Journal of Clinical Oncology*, sought to determine the prognostic and predictive impact of WHO-defined molecular subgroups and corresponding molecular alterations, known as IDH1/2 mutations, in people with the disease. LGG patients display highly variable survival outcomes depending on which molecular subgroup they are in. These subgroups are: IDH-wild type, IDH-mutant/1p19q non-codeleted, and IDH-mutant/1p19q codeleted. Genetic mutations were determined by testing patients' tissue samples through immunohistochemistry and/or deep sequencing.

A total of 116 of 251(46%) enrolled 'high-risk' patients with LGG from the two treatment arms had adequate tissues available for genomic analyses using multiple platforms. After neuropathology review, representative areas (70% tumor) were selected for DNA isolation. Of the eligible patients successfully profiled for the WHO-defined molecular groups, 26 of them (24%) were IDH-wild type, 43 (41%) were IDH-mutant/non-codeleted, and 37 (35%) were IDH-mutant/codeleted. Treatment with postradiation chemotherapy (PCV; procarbazine, lomustine (CCNU), and vincristine) was associated with longer progression-free survival (HR, 0.32; P =.003; HR, 0.13; P

"Our study is the first to our knowledge to demonstrate the predictive value of the WHO-defined molecular subgroups in a practice-changing phase III clinical trial of high-risk grade II glioma in correlation to overall survival with long-term follow-up data," said the study's lead author Arnab Chakravarti, MD, professor and chair of the Department of Radiation Oncology at The Ohio State University Comprehensive Cancer Center, the Klotz Family Chair of Cancer Research, and Director of the Brain Tumor Program. "Our evidence suggests that IDH mutation status could serve as the primary predictor of response to PCV in addition to radiotherapy in high-risk LGGs and is a more accurate

predictor of response than historical histopathological classifications."

Importantly, the analysis supports the notion that patients with IDH-mutant high risk LGG, regardless of codeletion status, receive benefit from the addition of PCV. "This study can now help clinicians interpret the results within the context of the altered molecular landscape and serve as a basis for survival times for the design of future high-risk LGG clinical trials," added Dr. Chakravarti.

More information: Bell EH et al. Comprehensive Genomic Analysis in NRG Oncology/RTOG 9802: A Phase III Trial of Radiation Versus Radiation Plus Procarbazine, Lomustine (CCNU), and Vincristine in High-Risk Low-Grade Glioma. J Clin Oncol, 2020 Jul 24;JCO1902983. DOI: 10.1200/JCO.19.02983.

Provided by NRG Oncology