Hippocampal avoidance during WBRT reduces risks in oncology trial

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Results from the NRG Oncology clinical study NRG-CC001 concluded that lowering radiotherapy dose to hippocampal stem cells improves cognitive and patient-reported outcomes for patients with brain

metastases. These findings were presented at Plenary Sessions at the 2018 Society for Neuro-Oncology (SNO) and the 2019 American Academy of Neurology (AAN) Annual Meetings and are now published in the *Journal of Clinical Oncology*.

"NRG-CC001 provides physicians with the information needed to offer patients a safer alternative to standard whole-brain radiotherapy. Hippocampal avoidance whole-brain radiotherapy with memantine should be a standard of care that providers offer for patients with brain metastases who are seeking whole-brain radiotherapy," stated Paul D. Brown, MD, of Mayo Clinic and co-lead author of the NRG-CC001 manuscript.

The NRG-C001 phase III trial enrolled 518 patients, which were randomly assigned to either receive whole-brain radiotherapy plus memantine with hippocampal avoidance or standard whole-brain radiotherapy plus memantine. The primary endpoint of the trial was cognitive function failure and the trial looked at secondary endpoints including overall survival, intracranial progression-free survival, toxicity, and patient-reported neurologic symptoms.

"Hippocampal avoidance during whole-brain radiotherapy in NRG-CC001 leads to a 26% relative reduction in cognitive toxicity risk following treatment. This is the first definitive and most important clinical evidence that the hippocampus is important in determining the negative effects that radiotherapy can have on cognitive function," added Vinai Gondi, MD, the Director of Research at the Northwestern Medicine Chicago Proton Center, Co-Director of the Brain Tumor Center at the Northwestern Medicine Cancer Center Warrenville, and co-lead author of the NRG-CC001 manuscript.

With a median follow up of 7.9 months, the risk of cognitive function failure was lower following hippocampal avoidance whole-brain

radiotherapy versus standard whole-brain radiotherapy (adjusted hazard ratio, 0.74, 95% confidence interval: 0.58-0.95, p=0.02). The difference was attributable to less deterioration in executive function at 4 months (23.3% vs. 40.4%, p=0.01) and learning and memory at 6 months (11.5% vs. 24.7%, p=0.049, and 16.4% vs. 33.3%, p=0.02, respectively). At 6 months, patients who received whole-brain radiotherapy with hippocampal avoidance reported less fatigue (p=0.04), less difficulty remembering things (p=0.01), and less difficulty speaking (p=0.0049), in addition to fewer cognitive symptoms (p=0.01) and less interference of neurologic symptoms in daily activities (p=0.008). There was no statistically significant difference between overall survival, intracranial progression-free survival, or toxicity between treatment arms.

More information: Paul D. Brown et al, Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients With Brain Metastases: Phase III Trial NRG Oncology CC001, *Journal of Clinical Oncology* (2020). DOI: 10.1200/JCO.19.02767

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