EMBARGO – 4:30pm (EDT)/ 1:30 (PST) – October 2, 2023

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Avoiding the hippocampus during prophylactic whole-brain radiotherapy prevents cognitive toxicity

New Study presented at ASTRO provides practice changing evidence

San Diego, CA – EMBARGO 4:50pm (EDT)/ 1:30pm (PST), October 2, 2023 – Prophylactic whole-brain radiotherapy can be delivered more safely to patients with small cell lung cancer by avoiding the hippocampus according to a randomized NRG Oncology trial presented at the American Society for Radiation Oncology (ASTRO) Annual Meeting.

Multiple clinical trials have shown that prophylactic whole-brain radiotherapy effectively prevents brain metastases and may prolong survival in small cell lung cancer. However, prophylactic whole-brain radiotherapy can lead to cognitive toxicity.

Vinai Gondi, MD, director of Radiation Oncology and co-director of the Brain Tumor Center at Northwestern Medicine Cancer Center Warrenville, and colleagues from the NRG Oncology Group, demonstrated in a prior phase III trial that avoiding the hippocampus during therapeutic whole-brain radiotherapy for patients with brain metastases can preserve cognitive function. In this trial of small cell lung cancer patients without brain metastases, they sought to determine if hippocampal avoidance had a similar cognitive benefit during prophylactic whole-brain radiotherapy.

To study the hypothesis that hippocampal avoidance could reduce neurocognitive decline during prophylactic whole-brain radiotherapy, 392 patients with small cell lung cancer and no radiographically evident brain metastases were randomized to prophylactic whole brain radiotherapy with or without hippocampal avoidance. Standardized cognitive tests were performed at baseline, 3, 6, 12, 18 and 24 months.

The results of the clinical trial found that the addition of hippocampal avoidance to prophylactic whole-brain radiotherapy for small cell lung cancer patients led to a 23% relative risk reduction in cognitive toxicity, non-inferior intracranial control, and similar survival.

“This study further supports our research on hippocampal avoidance in preventing radiation-related cognitive toxicity,” said Dr. Gondi, MD. “Hippocampal avoidance led to a similar risk reduction in cognitive toxicity during prophylactic whole-brain radiotherapy as it did with therapeutic whole-brain radiotherapy in our prior phase III trial NRG CC001. This finding demonstrates that the benefits of hippocampal avoidance are histology-agnostic and underscores the importance of preserving hippocampal neurogenesis during brain irradiation.”

Of the two types of lung cancer, small cell lung cancer is less common but spreads more aggressively to the brain than non-small cell cancers. Cancer will metastasize in the brain of 50 to 80 percent of small cell lung cancer patients. Due to concerns about cognitive toxicity, prophylactic whole brain radiotherapy is often not recommended to patients, in spite of its effectiveness in preventing brain metastases and prolonging survival.

“With advanced techniques such as intensity-modulated radiation therapy (IMRT) to reduce radiation dose to the hippocampus and preserve hippocampal neurogenesis, small cell lung cancer patients can now reap the benefits of prophylactic whole-brain radiotherapy with less toxicity,” said Dr. Gondi.

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