



# READ IT BEFORE YOUR PATIENTS

## Metastases

### Hippocampal Avoidance During Whole-Brain Radiotherapy Plus Memantine for Patients With Brain Metastases: Phase III Trial NRG Oncology CC001.

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#### PURPOSE:

A radiation dose to the neuroregenerative zone of the hippocampus has been found to be associated with cognitive toxicity. Hippocampal avoidance (HA) using intensity-modulated radiotherapy during whole-brain radiotherapy (WBRT) is hypothesised to preserve cognition.

#### METHODS:

This phase III trial enrolled adult patients with brain metastases to HA-WBRT plus memantine or WBRT plus memantine. The primary end-point was time to cognitive function failure, defined as decline using the reliable change index on at least one of the cognitive tests. Secondary end-points were overall survival (OS), intracranial progression-free survival (PFS), toxicity, and patient-reported symptom burden.

#### RESULTS:

Between July 2015 and March 2018, 518 patients were randomly assigned. Median follow-up for living patients was 7.9 months. Risk of cognitive failure was significantly lower after HA-WBRT plus memantine versus WBRT plus memantine (adjusted hazard ratio, 0.74; 95% CI, 0.58 to 0.95;  $P = .02$ ). This difference was attributable to less deterioration in executive function at four months (23.3% v 40.4%;  $P = .01$ ) and learning and memory at six months (11.5% v 24.7% [ $P = .049$ ] and 16.4% v 33.3% [ $P = .02$ ], respectively). Treatment arms did not differ significantly in OS, intracranial PFS, or toxicity. At six months, using all data, patients who received HA-WBRT plus memantine reported less fatigue ( $P = .04$ ), less difficulty with remembering things ( $P = .01$ ), and less difficulty with speaking ( $P = .049$ ) and, using imputed data, less interference of neurologic symptoms in daily activities ( $P = .008$ ) and fewer cognitive symptoms ( $P = .01$ ).

#### CONCLUSION:

HA-WBRT plus memantine better preserves cognitive function and patient-reported symptoms, with no difference in intracranial PFS and OS, and should be considered a standard-of-care for patients with good performance status who plan to receive WBRT for brain metastases with no metastases in the HA region.