

RTOG 0614: A Randomized, Phase III, Double-Blind, Placebo-Controlled Trial of Memantine for Prevention of Cognitive Dysfunction in Patients Receiving Whole-Brain Radiotherapy

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Background/Hypothesis

- WBRT is associated with cognitive impairment
 - At 4 months after RT, 60% of patients experience declines in ≥ 1 cognitive domain
- Mechanism similar to vascular and Alzheimer's
- Memantine improves cognition in mild to moderate vascular and Alzheimer's dementia
- Hypothesis: Memantine during and after WBRT for brain metastasis will prevent cognitive decline after radiotherapy



Schema/Assessment

WBRT 37.5Gy in 15 Fractions

Randomized to Memantine 20mg daily or Placebo within 3d of start of RT

Stratified by RPA class (I vs II)

MRI, Cognitive Assessment and QOL at Baseline, 8, 16, 24 and 52 Weeks

Cognitive domain	Measure
Memory	Hopkins Verbal Learning Test-Revised
Processing speed	Trail making test Part A
Executive function	Trail making test Part B, controlled oral word association
Global function	Mini-mental status examination
Cognitive function (self-report)	Medical outcomes scale – cognitive function scale
Quality of life	Fact-Br

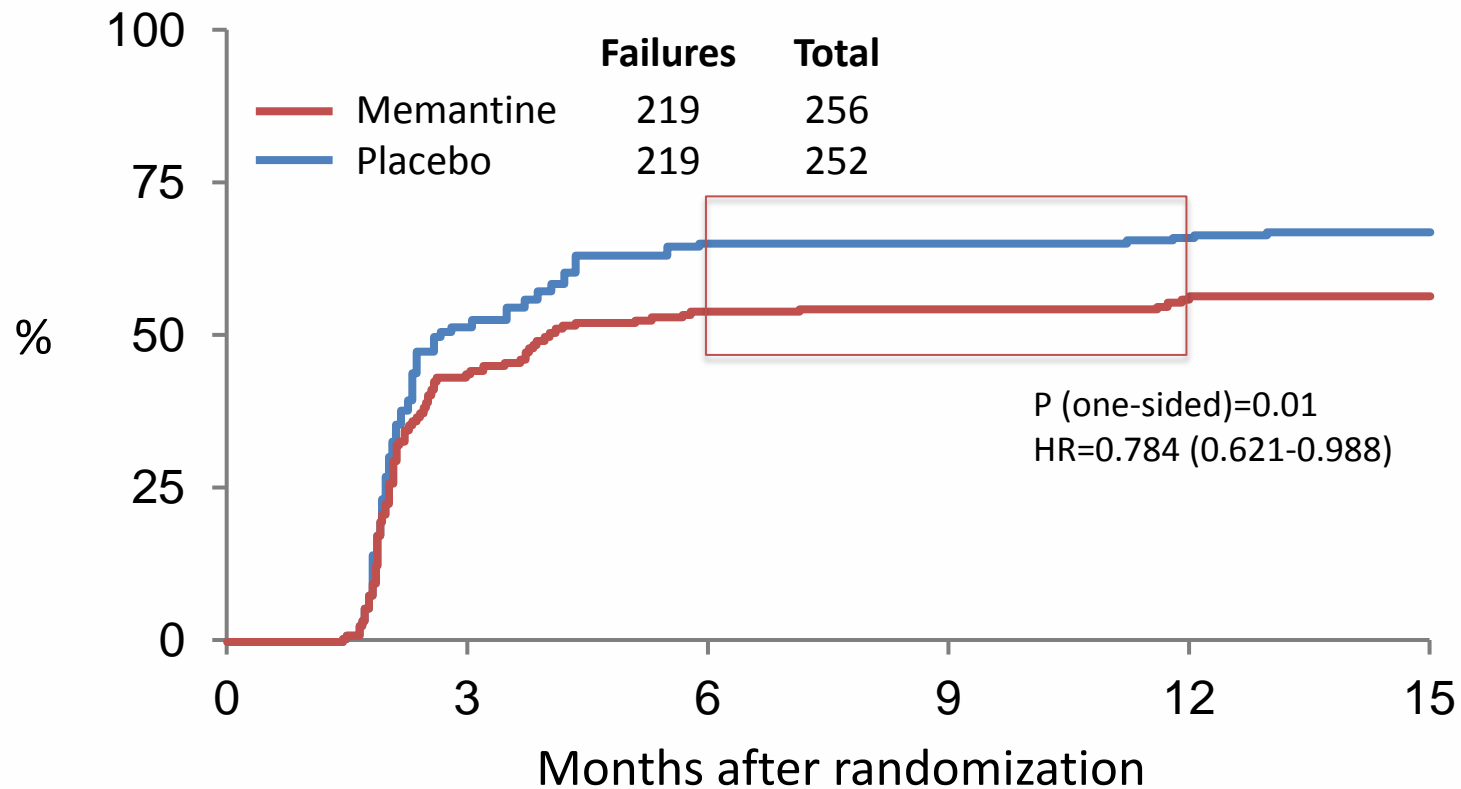


Patients/ Results

- 554 accrued (508 eligible) March 2008-June 2010
 - Median follow-up 12.4 months
 - No differences in OS (6m) or PFS (5m) were seen between arms
- Compliance similar between arms
 - Poorer than expected survival led to poor protocol compliance
 - 149 patients analyzable at 24 weeks
- Primary Objective: Memory (HVLt-R DR)
 - Memantine Reduced the decline in HVLt-R DR by 0.9 (SD)/2(Raw) (P=.059 due to patient loss) at 24 weeks
- Secondary Objective: Cognitive Function Decline/Failure
 - Change > RCI or 2SD decline from baseline for any test



Cognitive Function Failure



Patient at risk

—	75	33	27	15	9
—	66	25	19	12	9



Results/Conclusions

- Memantine
 - Reduced the decline in HVLT-R DR by 0.9 (P=.059 due to patient loss) at 24 weeks
 - 17% reduced relative risk of cognitive decline (p=.01)
 - » Maintained even after memantine stopped
 - Delayed time to cognitive decline (p=.01)
 - Reduced the rate of decline in cognitive, executive, and global function as well as processing speed (p<.01)
- Memantine helps to preserve cognitive function after WBRT in patients with brain metastases

