Int J Radiat Oncol Biol Phys. 2024 Jul 11:S0360-3016(24)00697-7. doi: 10.1016/j.ijrobp.2024.05.031.
Online ahead of print.

Memantine to Reduce Cognitive Impairment After Radiation in Children: A Pilot Study Evaluating the Feasibility of Memantine in Reducing Cognitive Impairment in Pediatric Patients after Radiation Therapy for Central Nervous System Tumors

Elizabeth L McKone [1], William G Breen [1], Nathan R Foster [2], Aaron W Bogan [3], Margaret A Connors [1], Reece A Alstat [4], Jonathan D Schwartz [5], Anita Mahajan [1], Safia K Ahmed [6], Nadia N Laack [7]

PMID: 39001719 DOI: 10.1016/j.ijrobp.2024.05.031

Abstract

Purpose: Memantine is standard in certain adults receiving brain radiation therapy (RT) to decrease cognitive impacts, but it is unknown whether pediatric patients can take, tolerate, and/or benefit from memantine. In this prospective single-arm feasibility study, we hypothesized that pediatric patients receiving central nervous system (CNS) RT would tolerate memantine with good adherence.

Methods and materials: Patients aged 4 to 18 years with a primary CNS malignancy (excluding World Health Organization grade 4 astrocytoma, glioblastoma) receiving intracranial RT were eligible. A 6-month memantine course was given during and after RT, with dose titration in 5 mg increments over 4 weeks targeting a weight-based maximum (0.4 mg/kg to the closest 5 mg), not to exceed 10 mg twice a day. The primary endpoint was to achieve 80% drug adherence rate in 80% of patients measured 1 month after RT. Secondary objectives included memantine feasibility at 3 and 6 months.

Results: Eighteen patients enrolled from 2020 to 2022 and were prescribed memantine with RT. The study closed early to avoid competing with the phase 3 randomized Children's Oncology Group study AACL2031. No predefined stopping rules were met. One patient withdrew for cognition-altering substance use, leaving 17 patients available for analysis. One patient discontinued memantine after one dose due to nausea. For the remaining 16 patients, there was a median of 100% pill completion rate (range, 74%-100%; n = 9/17 with 100% adherence) at 1 month after RT, with 15/16 (94%) with adherence rates >80%. At the 3- and 6-month post-RT time points for secondary endpoints, the median adherence rates were 100% (range, 55%-100%) and 96% (range, 33%-100%), respectively. Grade 1 to 2 fatigue, headache, and nausea were the most common toxicity events, at least possibly related to the study drug (n = 27), without attributable grade 3+ events.

Conclusions: Memantine is a feasible, safe, and well-tolerated addition to multimodality treatment for pediatric CNS malignancies. Results of "Anonymized for Review" are awaited to define the value of memantine in this population.