**Effect of Chemotherapy on Cognitive Function in Patients With Low-Grade Glioma**

The purpose of this prospective phase II/III trial was to study the effect of therapy intensification when combining procarbazine, lomustine, and vincristine (PCV) chemotherapy with a standard course of radiation therapy (RT) on cognitive functioning for patients with World Health Organization grade 2 low-grade gliomas (LGGs). Initial results of the trial demonstrated a progression-free survival benefit with adjuvant PCV, but no overall survival benefit in the intention-to-treat analysis. Because patients with LGGs have favorable prognostic indicators, the five-year overall survival rates range from 60%–70%. The effect of cancer treatment on neurocognitive function is a topic of increasing interest to healthcare providers and patients. The negative effect is commonly called “chemobrain” and refers to diminished concentration and compromised short-term memory following treatment. Chemobrain has been studied in other populations of patients with cancer (e.g., breast cancer) with associated statistically significant chemotherapy-associated compromised cognitive function when chemotherapy was added to RT.

This trial prospectively captured cognitive function evaluations for 362 patients with LGGs. Cognitive function was measured using the Folstein Mini-Mental State Examination (MMSE), which is a validated screening test for dementia and cognitive impairment. Scores on the MMSE range from 1–30, and higher scores indicate greater cognitive impairment. The purpose of the secondary analysis was to assess patterns of cognitive function changes post-treatment and to determine the potential for an untoward effect on cognitive function when chemotherapy is added to RT, when compared to RT alone. Of the 362 patients, 251 had World Health Organization grade 2 glioma and were either aged 40 years or older with any resection or younger than age 40 years with subtotal resection or biopsy. Those patients were randomly assigned to RT or RT plus PCV. The remaining 111 patients were younger than age 40 years with gross total resections, and those patients were observed. All participants were assessed by MMSE at baseline and at years 1, 2, 3, and 5 prospectively.

The results indicated that, with a gain or decline in the MMSE score, the majority of patients maintained their baseline cognitive function. Significant decline of MMSE score was rare, and those with a baseline MMSE score of less than 27 were more likely to experience significant gains in their MMSE score, which may have been caused by baseline deficits in cognitive function from the tumor that were reversed with therapy.

The authors cautioned that MMSE is an insensitive tool and has not been validated in patients receiving cranial RT. Therefore, the tool may not have identified changes in cognitive function in the study population. The authors concluded that the addition of PCV to RT for LGGs did not result in significant MMSE score decline when compared to RT alone during five years of follow-up. Additional findings demonstrated that patients in both study arms experienced a statistically significant increase in average MMSE score over time, with no difference in cognitive function. The authors suggested that enhanced neurocognitive assessments may detect subtle changes and should be used to supplement MMSE in future studies.

This study pointed to the importance of validating a more intensive treatment regimen for this patient population with high overall survival rates. Future studies also should assess the potential for serious compromised cognitive function outweighing the benefit of progression-free survival. By studying the association of the addition of PCV to RT with the effect on cognitive function, an enhanced decision-making process was facilitated for clinicians and patients.