

Originally published as JCO Early Release 10.1200/JCO.2006.06.2117 on July 24 2006

Journal of Clinical Oncology, Vol 24, No 24 (August 20), 2006: pp. 3865-3870

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High-Dose Chemotherapy With Autologous Stem-Cell Transplantation and Hyperfractionated Radiotherapy As First-Line Treatment of Primary CNS Lymphoma

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PURPOSE: To improve survival and reduce toxicity in primary CNS lymphoma (PCNSL) treatment, we conducted a multicenter phase II study with early high-dose chemotherapy (HDT) and autologous stem-cell transplantation (ASCT) followed by hyperfractionated whole-brain radiotherapy (WBRT) for newly diagnosed PCNSL patients younger than 65 years of age.

PATIENTS AND METHODS: Chemotherapy included three steps: three cycles of methotrexate (8 g/m²); cytarabine (AraC; two doses of 3 g/m²) and thiotepa (40 mg/m²) followed by stem-cell harvest; HDT with carmustine (400 mg/m²) and thiotepa (two doses of 5 mg/kg body weight) followed by ASCT. WBRT (45 Gy, two doses of 1 Gy/d) was administered for consolidation.

RESULTS: Thirty patients with PCNSL younger than 65 years of age (median, 54 years; range, 27 years to 64 years) were enrolled (nine pilot-phase; 21 phase II). Twenty-eight patients responded to methotrexate: six patients with complete remission (CR), 15 patients with partial remission (PR),

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and seven patients with stable disease (SD) with clinical improvement. Of 26 patients proceeding to AraC and thiotepa, 10 patients achieved CR, 14 patients achieved PR, one patient experienced SD with clinical improvement, and one patient suffered disease progression. Twenty-three patients received HDT plus ASCT, resulting in 15 patients with CRs and eight patients with PRs. After WBRT, 21 of 21 patients had CRs. One patient died from liver failure after methotrexate. HDT was well tolerated apart from WHO grade 3/4 cytopenia. With a median follow-up of 63 months (range, 4 months to 84 months), 5-year overall survival probability is 69% for all patients and 87% for the 23 patients receiving HDT plus ASCT. The 5-year probability of relapse-related death is 21% for all patients (n = 30) and 8.7% for patients treated with HDT plus ASCT (n = 23).

CONCLUSION: Sequential systemic methotrexate and AraC and thiotepa followed by HDT plus ASCT and hyperfractionated WBRT is very effective with little toxicity as initial therapy for PCNSL.

published online ahead of print at www.jco.org on July 24, 2006.

Presented in part at the 47th Annual Meeting of the American Society of Hematology, Atlanta, GA, December 10-13, 2005.

Authors' disclosures of potential conflicts of interest and author contributions are found at the end of this article.

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