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High-Dose Methotrexate Prolongs Life in Brain Lymphomas

BOSTON, Feb. 1 -- After nearly seven years, five of 12 patients maintained a complete response to treatment with high-dose methotrexate alone for a primary central nervous system lymphoma.

The updated results of a phase II, multicenter trial (NABTT, 1996-2007) that included 25 adult patients with newly diagnosed disease were reported by Tracy Batchelor, M.D., of Harvard, and colleagues in the Jan. 29 issue of Neurology.

Patients were treated with 8 g/m2 of IV methotrexate every two weeks until a complete response was reached (by radiographic criteria) or for four months, including a maximum of eight induction doses.

For patients achieving a complete response in that study, two consolidation cycles were given every 14 days followed by 11 maintenance cycles of 28 days each.

Median follow-up was 6.8 years.

Of the original 25 patients, 11 patients died of progressive disease or unknown causes and three died from other illnesses (two from cardiac disease, one from septic arthritis).

There were no methotrexate-related deaths, the researchers reported.

Median progression-free survival was 12.8 months (95% CI 3.5 to 37.2 months).

Multiple salvage regimens, as determined by the treating physicians, were used for relapses.

Of the relapsed patients, 13 received brain irradiation (12 had whole-brain irradiation and one had radiosurgery); Nine of these 13 died.

Six patients (24%) developed disease outside the central nervous system, three of whom died from systemic progression.

Median disease-specific survival had yet to be reached at six years (95% CI 37.7 months to not achieved), the researchers said.

Significantly, the researchers said, median overall survival for all patients who received methotrexate was 4.6 years (55.4 months).

In contrast, median overall survival for patients given whole-brain irradiation alone is reported to be one year (11.6 months), they wrote.

The methotrexate toxicity in this study was modest, the researchers said, with only 12 of 25 patients experiencing grade 3 or 4 toxicity after 287 cycles, with no episodes of clinically relevant leukoencephalopathy.

However, the optimal methotrexate-based combination regimen, as well as the duration of therapy, has yet to be defined, the researchers said.

They noted that progression-free survival in this study was shorter than that reported for some combination regimens in similar patients. Moreover, they said, the proportion of patients who experienced progression outside the central nervous system was higher than anticipated.

However, the researchers said, salvage therapy was successful with results comparing favorably with combination and radiation regimens.

This said, the researchers noted that high-dose methotrexate alone or in combination with other therapies is the most effective treatment available at present.

Future studies, they said, are needed to determine the combination regimen that will produce maximal efficacy and acceptable toxicity.