Phase II trial of lomustine plus temozolomide chemotherapy in addition to radiotherapy in newly diagnosed glioblastoma: UKT-03

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PURPOSE: To evaluate toxicity and efficacy of the combination of lomustine, temozolomide (TMZ) and involved-field radiotherapy in patients with newly diagnosed glioblastoma (GBM).

PATIENTS AND METHODS: Thirty-one adult patients (median Karnofsky performance score 90; median age, 51 years) accrued in two centers received involved-field radiotherapy (60 Gy in 2-Gy fractions) and chemotherapy with lomustine 100 mg/m² (day 1) and TMZ 100 mg/m²/d (days 2 to 6) with individual dose adjustments according to hematologic toxicity.

RESULTS: A median of five courses (range, one to six courses) were delivered. WHO grade 4 hematotoxicity was observed in five patients (16%) and one of these patients died as a result of septicemia. Nonhematologic toxicity included one patient with WHO grade 4 drug-induced hepatitis (leading to discontinuation of lomustine and TMZ) and one patient with WHO grade 2 lung fibrosis (leading to discontinuation of lomustine). The progression-free survival (PFS) rate at 6 months was 61.3%. The median PFS was 9 months (95% CI, 5.3 to 11.7 months), the median overall survival time (MST) was 22.6 months (95% CI, 12.5 to not assessable), the 2-year survival rate was 44.7%. O6-methylguanine-DNA methyltransferase (MGMT) gene-promoter methylation in the tumor tissue was associated with longer PFS (P = .014, log-rank test) and MST (P = .037).

CONCLUSION: The combination of lomustine, TMZ, and radiotherapy had acceptable toxicity and yielded promising survival data in patients with newly diagnosed GBM. MGMT gene-promoter methylation was a strong predictor of survival.

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