

University of Texas M. D. Anderson Cancer Center, Houston, USA. jaeckle.kurt@mayo.edu.

Abstract

PURPOSE: Temozolomide (TMZ) and 13-cis-retinoic acid (cRA) have shown activity in prior single-agent trials of recurrent malignant gliomas (MG). This phase II trial evaluated efficacy and toxicity of combination temozolomide and cRA treatment in recurrent MG.

PATIENTS AND METHODS: Adults with recurrent supratentorial MG for whom surgery, radiation, and/or chemotherapy failed were eligible. Treatment included oral TMZ 150 or 200 mg/m2/d, days 1 through 5, and cRA 100 mg/m2/d, days 1 to 21, every 28 days. Primary end point was progression-free survival at 6 months (PFS 6); secondary end points included response, survival, and PFS12.

RESULTS: Eighty-eight eligible patients (glioblastoma multiforme \[n = 40\]; anaplastic gliomas \[n = 48; astrocytoma, 28; oligodendroglioma, 14; mixed glioma, six\]) received treatment. PFS 6 was 43\% (95\% confidence interval [CI], 33\% to 54\%) and PFS12 was 16\% (95\% CI, 10\% to 26\%). Median overall PFS was 19 weeks (95\% CI, 16 to 27 weeks), and median overall survival (OS) was 47 weeks (95\% CI, 36 to 58 weeks). OS was 46\% (95\% CI, 36\% to 57\%) at 52 weeks and 21\% (95\% CI, 13\% to 31\%) at 104 weeks. Of 84 assessable patients, there were two (3\%) complete responses and eight (12\%) partial responses (complete plus partial response, 15\%). Among 499 treatment cycles, the most common grade 3/4 events included granulocytopenia (1.8\%), thrombocytopenia (1.4\%), and hypertriglyceridemia (1.2\%).

CONCLUSION: TMZ and cRA were active, exceeding our 20\% thresholds for PFS 6 success, assuming 20\% improvement over our previously reported database (glioblastoma multiforme: expected, 30\%; observed, 32\%; anaplastic glioma: expected, 40\%; observed, 50\%).

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