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Temozolomide and cisplatin versus temozolomide in patients with advanced melanoma: a randomized phase II study of the Hellenic Cooperative Oncology Group.

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Source

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Abstract

PURPOSE:

Temozolomide (TMZ) is an oral alkylating agent that produces methyl adducts at the 0.6 position of guanine. The methyl adducts are removed by the DNA repair enzyme AGAT. As demonstrated by in vitro studies, cisplatin (CDDP) is able to down-regulate the AGAT activity, suggesting that CDDP could enhance the antitumor activity of TMZ. We designed a randomized phase II study to evaluate and compare the activity and safety profile of the combination versus single-agent TMZ in patients with advanced melanoma.

PATIENTS AND METHODS:

From January 2000 to April 2002, 132 patients were enrolled on the study. Patient and tumor characteristics were well balanced between the two arms. Patients with cerebral metastases were included. Patients received TMZ 200 mg/m(2)/day orally for five consecutive days every 4 weeks or TMZ + CDDP 200 mg/m(2) daily on days 1-5 and 75 mg/m(2) of CDDP on day 1.

RESULTS:

Tumor responses (complete and partial responses) were seen in 16 patients (26%) in arm A and 19 patients (29%) in arm B. The median time to progression (TTP) was 3.8 months in arm A and 5.8 months in arm B. The median overall survival (OS) was 11.5 months in arm A and 12 months in arm B. The difference between treatment arms regarding objective response rates, TTP and OS were not statistically significant. Toxicity was comparable between the two arms for anemia, leukopenia, neutropenia, thrombocytopenia, fatigue, constipation and arthralgias/myalgias. There was significantly more grade 3 and 4 emesis in the combination arm.

CONCLUSIONS:

No clear benefit in terms of response rates, median TTP or OS was shown with the combination of TMZ + CDDP. Additionally, the combination was associated with higher incidence of grade 3 and 4 emesis.