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Temozolomide in combination with celecoxib in patients with advanced melanoma. A phase II study of the Hellenic Cooperative Oncology Group.

Gogas H, Polyzos A, Stavrinidis I, Frangia K, Tsoutsos D, Panagiotou P, Markopoulos C, Papadopoulos O, Pectasides D, Mantzourani M, Middleton M, Vaiopoulos G, Fountzilas G.

Source

First Department of Medicine, University of Athens, Medical School, Athens, Greece. hgogas@hol.gr

Abstract

BACKGROUND:

There is now increasing evidence that a constitutive expression of cyclooxygenase (COX)-2 plays a role in the development and progression of malignant epithelial tumors. Expression of COX-2 is seen in 93% of melanomas, as determined by immunohistochemistry. Temozolomide (TMZ) has demonstrated activity against melanoma and has been investigated as single agent or in combination. We designed a phase II study to assess the efficacy and toxicity of the combination of TMZ and celecoxib (a COX-2 inhibitor) in patients with advanced melanoma.

PATIENTS AND METHODS:

From January 2003 to July 2004, 52 patients were enrolled in the study. Nineteen patients were M1a, six M1b and 27 M1c. Patients received TMZ 200 mg/m(2) per day p.o. for 5 consecutive days every 4 weeks and celecoxib 400 mg b.i.d. p.o. for a maximum of six cycles. Celecoxib was continued until progression.

RESULTS:

The median age was 63 years. There were 29 males and 23 females. Among 50 assessable patients, there were 11 (21.5%) objective responses including five complete responses and six partial responses. Twenty patients (38.5%) had stabilization of their disease, and 19 (36.5%) progressed. The median time to progression was 4.6 months and the median survival 9.5 months. Twenty-two patients (41.5%) completed all cycles of treatment. Median relative dose intensity of TMZ was 0.99 (range 0.6-1.2). Most commonly seen toxic effects included anemia (27.5%), neutropenia (17.5%), thrombocytopenia (33%), nausea/vomiting (75%), gastrointestinal (52%) and fatigue (46.5%). One patient discontinued due to severe toxicity. COX-2 was determined by immunohistochemistry and was expressed in all cases.

CONCLUSION:

The combination of TMZ and celecoxib is safe and potentially effective in the treatment of metastatic melanoma. Randomized studies are needed to explore the role of celecoxib in combination with chemotherapy or as maintenance treatment in these patients.