Treatment of recurrent malignant gliomas with high-dose 13-cis-retinoic acid.

Yung WK, Kyritsis AP, Gleason MJ, Levin VA.
Department of Neuro-Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas 77030, USA.

Abstract
Malignant gliomas account for more than 60% of all primary brain tumors in adults. Adjuvant chemotherapy in addition to radical surgery and radiation therapy has provided only a modest increase in survival. Retinoic acid has been shown to have growth-inhibitory activity against glioma cells in culture. This provides the rationale for a Phase II study using 13-cis-retinoic acid (CRA) in patients with recurrent malignant brain tumors. The objective of this study was to determine the clinical activity of CRA in patients with a histologically proven diagnosis of malignant brain tumor and documented progressive or recurrent disease after radiation and chemotherapy. Fifty patients with documented recurrent disease were treated with CRA as a single agent p.o. at a dose of 60-100 mg/m² per day. Three weeks of treatment were followed by 1 week of rest. Of the 43 patients who received more than 4 weeks of therapy, 3 (7%) achieved partial response, 7 (16%) achieved minor response, 13 (30%) remained stable, and 20 (47%) had disease progression. The median time from onset of treatment to disease progression for the whole group of 43 patients was 16 weeks (19 weeks for glioblastomas and 11 weeks for anaplastic glioma), whereas that for the 23 patients with partial response and minor response and who remained stable was 66 weeks, and that for the 20 patients with progressive disease was only 8 weeks. The median survival time for glioblastoma was 58 weeks, and 34 weeks for anaplastic astrocytoma. Toxicity was mainly dermatological, with dry skin and cheilitis. These preliminary results suggest that 13-cis-retinoic acid is active against malignant gliomas and is very well tolerated.