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Combination chemotherapy with 13-cis-retinoic acid and celecoxib in the treatment of glioblastoma multiforme.

Levin VA, Giglio P, Puduvali VK, Jochev J, Groves MD, Yung WK, Hess K.

Neuro-Oncology Unit 431, Department of Neuro-Oncology, The University of Texas M. D. Anderson Cancer Center, Houston, Texas 77230-1402, USA. vlevin@mdanderson.org

Abstract

In a phase II clinical trial, we sought to determine if combining celecoxib with 13-cis-retinoic acid (13-cRA, Accutane) was efficacious in the treatment of recurrent (progressive) glioblastoma multiforme (GBM). In parallel, we also sought to determine to what extent the outcomes from this clinical trial correlated with the findings from studies utilizing two murine intracerebral GBM models, U87MG and U251HF, to determine the predictive value of these murine models. In the clinical trial, 25 patients were studied at recurrence. Stable disease, which occurred in 44% of the patients, was the best response. The median progression-free survival (PFS) was 8 weeks, with a PFS at 6 months of only 19%. For the patients with stable disease, the median PFS was 24 weeks. The toxicity profile was unremarkable. The modest effect on PFS seen in this study agreed with the recent findings of another study, which showed a 19% PFS at 6 months in patients treated with 13-cRA alone. Thus, the combination of 13-cRA with celecoxib is not more effective than 13-cRA in the treatment of progressive GBM. In the murine model study, we found that long-term dosing with 13-cRA or celecoxib alone or in combination did not increase survival in animals with U87MG tumors but modestly increased survival in animals with U251HF tumors. There was no evidence of synergism between the two drugs. From this, we concluded that the animal studies generally predicted that the two agents would have only a modest effect alone and no additive effect when given in combination to patients.

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