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1: J Neurosurg. 2005 Apr;102(4):706-14. Related Articles, Links

Combined cimetidine and temozolomide, compared with temozolomide alone: significant increases in survival in nude mice bearing U373 human glioblastoma multiforme orthotopic xenografts.

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OBJECT: Malignant gliomas consist of both heterogeneous proliferating and migrating cell subpopulations, with migrating glioma cells exhibiting less sensitivity to antiproliferative or proapoptotic drugs than proliferative cells. Therefore, the authors combined cimetidine, an antiinflammatory agent already proven to act against migrating epithelial cancer cells, with temozolomide to determine whether the combination induces antitumor activities in experimental orthotopic human gliomas compared with the effects of temozolomide alone. METHODS: Cimetidine added to temozolomide compared with temozolomide alone induced survival benefits in nude mice with U373 human glioblastoma multiforme (GBM) cells orthotopically xenografted in the brain. Computer-assisted phase-contrast microscopy analyses of 9L rat and U373 human GBM cells showed that cimetidine significantly decreased the migration levels of these tumor cells in vitro at concentrations at which tumor growth levels were not modified (as revealed on monotetrazolium colorimetric assay). Computer-assisted microscope analyses of neoglycoconjugate-based glycohistochemical staining profiles of 9L gliosarcomas grown in vivo revealed that cimetidine significantly decreased expression levels of endogenous receptors for fucose and, to a lesser extent, for N-acetyl-lactosamine moieties. Endogenous receptors of this specificity are known to play important roles in adhesion and migration processes of brain tumor cells. CONCLUSIONS: Cimetidine, acting as an antiadhesive and therefore an antimigratory agent for glioma cells, could be added in complement to the cytotoxic temozolomide compound to combat both migrating and proliferating cells in GBM.

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