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Clinical Investigations

Effect of phenytoin on celecoxib pharmacokinetics in patients with glioblastoma

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▶ Abstract

Cyclooxygenase-2 (COX-2) expression has been linked to the prognosis, angiogenesis, and radiation sensitivity of many malignancies. Celecoxib, a selective COX-2 inhibitor, is predominantly eliminated by hepatic metabolism. This study was conducted to determine the effects of hepatic enzyme-inducing antiseizure drugs (EIASDs) on the pharmacokinetics of celecoxib. The safety of celecoxib administered with radiation for glioblastoma and the effect of the combined treatment on survival were also evaluated. Patients were stratified based on concomitant use of EIASDs. Celecoxib (400) mg was administered orally twice a day until tumor progression or dose-limiting toxicity. Standard radiation was administered

without adjuvant chemotherapy. Sampling was performed to define the plasma concentration/time profile for the initial dose of celecoxib and steady-state trough concentrations. Thirty-five patients (22 +EIASD, 13 -EIASD) were enrolled. There were no significant differences in age, performance status, extent of surgery, or Mini Mental State Exam scores between the two cohorts. The treatment was well tolerated. All patients in the +EIASD arm were taking phenytoin. There were no significant differences in any celecoxib pharmacokinetic parameters between 15 +EIASD and 12 -EIASD patients. With 31 of 35 patients deceased, estimated median survival time for all patients was 12 months (+EIASD, 11.5 months; -EIASD, 16 months; $p = 0.11$). The pharmacokinetics of celecoxib is not significantly affected by the concomitant administration of phenytoin. Celecoxib administered during and after radiation is well tolerated. The potential difference in survival between the +EIASD and -EIASD groups deserves further evaluation.

Key Words: celecoxib, COX-2 inhibitor, enzyme-inducing anticonvulsants, glioblastoma multiforme, pharmacology, radiation therapy, survival

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