

A Study of The Pharmacokinetic Effects Of Cyclophosphamide On Medulloblastoma Patients

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Medulloblastoma is a malignant solid brain and spinal tumor that is most commonly found in the posterior fossa, which accounts for 20% of childhood brain tumors. Cyclophosphamide is an anti-tumor prodrug that is currently used for the treatment of solid tumors. This drug must be broken down into the active metabolite hydroxycyclophosphamide in the liver by hepatic enzymes, cytochrome P450 CYP3A5 and CYP2C9 enzymes. Polymorphisms in the CYP3A5 and CYP2C9 subfamilies affect cyclophosphamide breakdown. Specifically, the polymorphisms CYP3A5*3 and *6 cause almost no enzyme to be produced and CYP2C9*2 causes a decreased production of enzymes, while the *1 genotype (wild-type) allows for normal enzyme productivity. In this study, St. Jude Children's Research Hospital patients' (n= 39) genotype were analyzed using polymerase chain reaction (PCR) and DdeI and AvaII restriction analysis. The genotypic allele frequencies were compared using a Chi Square test to previously existing CYP3A5 and CYP2C9 studies. There was no statistical difference in p-values when the allele frequencies were compared to these other CYP3A5 and CYP2C9 studies meaning that our genotypic results are consistent for a given population. In future studies, this genotypic information will be correlated with pharmacogenetic information regarding cyclophosphamide treatment-based protocols for these patients. By knowing each patient genotype in regard to the cytochrome P450 hepatic enzymes CYP3A5*3 and *6 and CYP2C9*2 polymorphisms, cyclophosphamide dosage may be specifically altered on a patient to patient scale.