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Clinical Trials in Urinary Bladder Cancer – Translation from Dogs to Humans (5-Sep-2003)

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Cancer is a major cause of morbidity and mortality in pet dogs and humans. Approximately 25% of humans and approximately 30% of older dogs in most breeds will develop cancer during their lifetime. Therapy remains ineffective for many forms of cancer. A long standing approach to "find" new cancer therapies for pet animals has been to "adapt" therapies currently in use in humans for use in dogs. While this flow of information from humans to dogs has provided some benefit to pet animals, it may be much more important to pet animals and to humans to design studies in which new information is generated in dogs and then flows from dogs to humans. Our group is pursuing this approach in studies of invasive urinary bladder cancer. Naturally-occurring canine transitional cell carcinoma (TCC) of the urinary bladder closely mimics invasive urinary bladder cancer in humans in histopathologic characteristics, biologic behavior, and response (or lack thereof) to therapy. Survival with TCC metastasis is typically less than one year in humans and less than 110 days in dogs. A novel therapy approach for TCC being studied by our group is the use of cyclooxygenase (cox) inhibitors as antitumor agents in TCC. Cox-2 is expressed in the majority of canine and human TCC cases. Single agent piroxicam (which inhibits the activity of cox-1 and cox-2) has been given to 62 dogs with TCC in clinical trials. Tumor responses have included: 2 complete remission, 9 partial remission ($\geq 50\%$ reduction in tumor volume), 35 stable disease ($< 50\%$ change in tumor volume), and 16 progressive disease ($\geq 50\%$ increase in tumor volume or new tumor lesions). The remission rate and stable disease rate are as good as or better than those for chemotherapy. These canine studies have led to 2 clinical trials of cox inhibitors in people with urinary bladder cancer at Indiana University (Dr. R. Foster, PI). In one trial, patients with carcinoma in situ (high grade cancer which has not yet invaded) are being treated with piroxicam after failing to respond to traditional medical therapy. Of 5 patients enrolled to date, 2 have had complete remission of their cancer. In a second clinical trial, patients who already have invasive TCC are being treated with a cox-2 inhibitor between diagnosis and cystectomy (cystectomy is standard treatment of invasive TCC in humans). The primary endpoint in this trial, induction of apoptosis (which was selected from canine studies), has been noted in 3 of 5 patients enrolled to date. In conclusion, studies of cox inhibitor therapy in TCC demonstrate how important information gained in canine studies can be of benefit to pet dogs and to humans with cancer. Supported by Morris Animal Foundation and National Institutes of Health.

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