Exploratory study of an oral blood-brain barrier penetrant, procaspase-3 activator (PAC-1) in combination with hydroxyurea for treatment of canine meningioma

Purpose
To determine whether treatment with the oral chemotherapy drug procaspase-3 activator (PAC-1), in combination with the oral drug hydroxyurea, can provide safe and effective treatment of canine meningiomas

Background
Brain tumors are a significant cause of illness and death in dogs, with meningioma accounting for approximately half of the cases diagnosed in pet dogs. Although surgery remains the best treatment dogs with meningioma, some dogs are not good candidates for this. In these situations, effective treatment options are limited. To address this gap, we are running a pilot clinical study to determine the safety and effectiveness of a new chemotherapy approach. Dogs in this study will receive an experimental combination of PAC-1 and hydroxyurea, followed by surgery to remove their tumor. Tumors will be analyzed to see if the drug combination was effective in reaching and targeting their tumors. We hope to determine if the experimental drug combination can provide an alternative treatment for dogs whose tumors cannot be surgically removed.

Eligibility
- Dogs of any breed, age, or sex
- MRI-confirmed diagnosis of a solitary, extra-axial forebrain mass lesion with imaging characteristics consistent with a meningioma (cerebral convexity, falcine, parasagittal) that is amenable to surgical resection.
- Measurable tumor (>10 mm diameter)
- Stable or decreasing dose of corticosteroids, and if applicable, seizures controlled with antiepileptic medication

Exclusion
- Dogs with significant preexisting renal, hepatic or cardiac disease, a history of poor performance under general anesthesia, or a history of prior radiotherapy or use of cytotoxic chemotherapy
- Dogs with cystic olfactory lobe lesions
- Dogs with uncontrolled seizures

Study Design
Enrolled dogs will have an initial visit including physical exam and bloodwork at the Veterinary Teaching Hospital in Blacksburg, VA. Dogs will begin taking oral prednisone, if they are not already receiving it. Interim rechecks will be performed in Blacksburg on Days 11 (including MRI), 28, and 40 (including MRI). The investigational treatment in this study is a combination of oral chemotherapy agents (PAC-1 + hydroxyurea), which will be administered at home by the owner beginning at approximately Day 15. Dogs will travel twice to the NIH National Cancer Institute in Bethesda, MD to have the chemotherapy treatment monitored with non-invasive molecular brain imaging techniques. At the conclusion of the study period (approximately Day 43), dogs will undergo surgical tumor removal. Dogs will be hospitalized for a total of 3-5 days for tumor removal.

Please note: PET scans at approximately Day 15 and Day 42 days post-treatment will take place at the NIH National Cancer Institute facility in Bethesda, MD.

The following is a sample visit schedule. The dates may be adjusted based on national holidays and hospital/NIH schedules. Owners must commit to presenting enrolled dogs for all required visits:

Day 1  | Enrollment visit | Veterinary Teaching Hospital, Blacksburg, VA
Day 11 | Recheck visit with MRI | Veterinary Teaching Hospital, Blacksburg, VA
Day 15 | PET/CT scan | NIH, NCI, Bethesda, MD
Day 28 | Recheck visit | Veterinary Teaching Hospital, Blacksburg, VA
Day 40 | Recheck visit with MRI | Veterinary Teaching Hospital, Blacksburg, VA
Day 42 | PET/CT scan | NIH, NCI, Bethesda, MD
Day 43-45 | Tumor removal surgery | Veterinary Teaching Hospital, Blacksburg, VA
Compensation

Owner is responsible for the cost of obtaining an MRI to confirm diagnosis. Once the diagnosis is confirmed and the dog is enrolled, all treatment and follow-up examinations related to this study will be provided at no cost during the study period. Owners are responsible for travel-related expenses and medication costs associated with ongoing seizure control, if required.

Contact

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