Funding for Studies of Childhood Sarcoma

A program of project grants led by a team of investigators from Nationwide Children’s Hospital, The Ohio State University College of Medicine and College of Veterinary Medicine has just received notice of an award from the National Institutes of Health. This effort is supported by the Comparative Animal Core led by Dr. Cheryl London, Department of Veterinary Biosciences. The core includes faculty from the Department of Veterinary Biosciences (Drs. Krista La Perle, Brad Bolon, Tracey Papenfuss) and Veterinary Clinical Sciences (Dr. Matthew Allen). Total direct costs supporting the core is approximately $750,000.

The purpose of this program project grant is to integrate efforts to generate a more complete understanding of signaling pathways in childhood sarcomas and develop novel therapeutic approaches. Approximately 70% of children with sarcomas can be cured using multimodality treatments but the outcome is still poor for those with advanced or metastatic disease. Specifically, fewer than 30% of children with advanced or metastatic Ewing sarcoma, osteosarcoma or rhabdomyosarcoma will survive past five years. Intensive treatments with chemotherapy and radiation therapy have not significantly altered this outcome over the past two decades. Specifically, the overarching goals are to comprehensively understand the roles of three signaling pathways (NF-kB, STAT3, and insulin like growth factors) in the maintenance of malignant phenotypes of childhood sarcomas, and based on this information develop novel and effective new therapies for treating patients. The combined expertise in childhood sarcoma biology of the principal investigators (Drs. Houghton, Guttridge and Lin) will help to integrate efforts across these signaling pathways and lay the groundwork for clinical evaluation of treatment approaches in dogs with sarcoma (i.e., osteosarcoma) as a prelude to human studies.

The primary objective of the Comparative Animal Core is to assist investigators in determining both the toxicities and activity associated with novel therapeutic approaches in mouse models of sarcoma, to identify candidate drugs/treatments that are likely to have success in the clinical setting, and to evaluate these treatments in dogs with spontaneous sarcomas as a prelude to future human clinical trials. This Core is housed and coordinated in the Department of Veterinary Biosciences in the College of Veterinary Medicine and includes individuals with expertise in comparative pathology, tissue banking, and clinical trial development and execution. Additionally, this Core provides support for two members of the Clinical Trials Office during the course of the preclinical and clinical studies.
The effects of preemptive analgesia with NSAIDs or tramadol in dogs undergoing cutaneous tumor removal

PURPOSE OF STUDY
The purpose of this study is to test if dogs with tumors benefit from treatment with pain medications prior to removal of those tumors.

Background
Cancer is highly prevalent among dogs; over 50% of dogs over 10 years of age die from or are euthanized due to cancer. Studies in human oncology patients have shown that 30-50% of cancer patients will experience moderate to severe pain. Tramadol is widely used in human and veterinary medicine for mild to moderate pain relief. Cancer pain can be characterized by components of bone, visceral and neuropathic pain, and many patients have central as well as peripheral sensitization. The World Health Organization considers NSAIDs to be the first tier of pain control in cancer patients, as inflammation is a major component of oncologic pain. Common side effects of NSAIDs in dogs are GI toxicity, impairment of renal blood flow, hepatopathy and impairment of coagulation. Thus, preoperative administration of NSAIDs is not appropriate for many oncologic patients. One study demonstrated that preemptive use of gabapentin for forelimb amputations in greyhounds with osteosarcoma was ineffective. The pharmacologic activity of tramadol includes weak mu opioid receptor agonism, inhibition of norepinephrine and serotonin reuptake and inhibition of 5HT reuptake. Thus, tramadol can potentially provide pain control at multiple points in the pain pathway, including the inflammatory pathway via inhibition of 5HT reuptake. Studies in human oncologic patients have shown that preemptive use of tramadol can reduce postoperative analgesia requirements. To date, no studies have compared the efficacy of NSAIDs to tramadol in veterinary oncologic patients.

INCLUSION CRITERIA
• Dogs with diagnosed skin tumors(sarcoma, carcinoma, melanoma, histiocytic sarcoma) are eligible for enrollment. Must be a low-risk anesthetic candidate as determined by a veterinary cardiologist.
• Dogs must not currently be receiving any nonsteroidal anti-inflammatory drugs (NSAIDs), steroids or pain medications.
• Dogs must be free from any serious underlying disorder (i.e., kidney, liver or heart disease).

STUDY DESIGN
Your dog will need to have diagnosis of a skin tumor (sarcoma, carcinoma, melanoma, histiocytic sarcoma, mast cell tumor) to participate in this study. Initially your dog will undergo a series of diagnostic tests, which may include blood tests, urinalysis, needle aspirations of the tumor and lymph nodes, chest x-rays/ultrasound and examination of the abdomen. The results of these initial staging tests will determine if your dog is eligible to enter this clinical trial. These tests are routinely performed when evaluating dogs with skin tumors. Once your dog has been deemed eligible to enter the study, he/she will be randomized to receive no treatment, an NSAID, or a low level narcotic for two days prior to surgery. You will also be required to complete a survey that helps to categorize your dog’s pain before treatment, prior to surgery, and post-surgery. Lastly, your dog’s pain will be assessed by study team members before and after treatment.

CLIENT COMPENSATION
Clients participating in this study will be given special financial considerations. The study will pay for preoperative pain medication, the initial oncology consultation, preoperative diagnostics and a portion of the subsequent surgery up to a total of $1000. Clients will be responsible for all additional costs.

CONTACT INFORMATION
Phillip Lerche, BVSc, PhD, DACVA
Nicole Karrasch, DVM Nicole.Karrasch@cvm.osu.edu
### COTC007b: Preclinical Comparison of Three Indenoisoquinolines Candidates in Tumor Bearing Dogs

Lymphoma is one of the most common cancers in dogs, accounting for 7% to 24% of all canine cancers. Although most dogs with lymphoma respond initially to current chemotherapy drugs, most eventually develop drug resistance. This clinical trial sponsored by the National Cancer Institute (NCI) assesses the safety and effectiveness of three newly developed chemotherapy agents (indenoisoquinolines) when given to dogs with lymphoma. Although this class of compounds has shown efficacy in a variety of cancers, indenoisoquinolines, are currently being evaluated in human patients as agents with improved drug stability and measurable blood levels. This study is the first time the indenoisoquinolines are being assessed in dogs with cancer. This trial is divided into 2 phases. The first phase is a dose finding phase to determine safety followed by a validation phase for biological assay development (tumor marker evaluation pre and post treatment). Anti-cancer activity against canine lymphoma will be assessed in both phases.

**PATIENT ELIGIBILITY CRITERIA:**

Dogs with confirmed diagnosis of lymphoma with at least one lymph node larger than 3 cm diameter are eligible to participate. Dogs may be newly diagnosed or have previously received treatment. A two week washout period from previous chemotherapy or radiation therapy is required and dogs must not have received corticosteroids or L-asparaginase seven days prior to entry into the study. Dogs must be feeling well and otherwise be in good overall health with adequate organ function, as determined by recent blood work, to participate in this study. Study period is 29 days with visits on days 1, 3, 5, 8, 15, 22 and 29.

**FINANCIAL INCENTIVES**

Once enrolled in this study, all costs associated with that study will be covered. Adverse events and unanticipated hospitalizations are also covered. Once the study has been completed, a $1000 credit will be applied to your dog’s account at the OSU Veterinary Medical Center which can be used for further treatment.

For more information please contact the Clinical Trials Office at 614-688-5713 or 614-247-8706 clinicaltrials@cvm.osu.edu

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### Brainstem Auditory-Evoked Response Testing In Normal Hearing Cavalier King Charles Spaniel Dogs

**OVERVIEW OF THE STUDY:**

Hearing disorders are a common condition recognized in many breeds of dogs. In the dog breed Cavalier King Charles Spaniel (CKCS), hearing disorders may be due to conductive hearing loss, which may occur with primary secretory otitis media (PSOM), or due to sensorineural hearing loss, which may occur when there is damage or an abnormality of the sensory cells in the cochlea or the auditory nerve. Evaluation of a dog’s hearing ability is done using the brainstem auditory evoked response (BAER) test. However, in order to identify an abnormality on the BAER test, the results from an individual dog must be compared to normal BAER values.

**PURPOSE OF THE STUDY:**

The purpose of this study is to obtain BAER data from CKCS dogs between the ages of 1 to 2 years old with no history of hearing loss. This is a 2-day study. Procedures performed include hearing testing (BAER test), a Computed Tomography (CT) scan and Magnetic Resonance Imaging (MRI); study pays for all testing.

Enrollment of dogs in the study has begun. If you are interested in possibly enrolling your CKCS dog in the study, please contact Dr. Cole at the telephone number or email address listed below. A pedigree is required for entry into the study, but will be kept confidential, as will all test results. Details of the study will be given individually on the phone or via email.

**CONTACT:**

Dr. Lynette Cole DVM, MS, Dipl. ACVD Dermatology and Otology Service Veterinary Medical Center Tel: (614) 292-3551 Email: cole.143@osu.edu
Utility and Repeatability of Quantitative Outcome Measures to Assess Recovery after Canine Spinal Cord Injury (SCI)

PURPOSE OF STUDY
The purpose of this study is to adapt several tests of sensory and motor function commonly used in rodent SCI models for dogs and to assess the utility and reliability of these tests in measuring recovery from SCI in dogs.

BACKGROUND
There is a high incidence of SCI in the general canine population, leading to a recent surge of clinical trials evaluating treatments to improve outcome. However, many clinical trials have difficulty identifying treatment effects because of a lack of sensitive and quantifiable measures to document sensory and motor recovery in dogs with SCI. There is a critical need for the development of sensitive and reliable outcome measures to assess recovery in dogs with SCI. Without reliable outcome measures, small-scale clinical trials are unlikely to identify modest but important treatment affects that would lead to larger-scale trials to benefit dogs with SCI.

INCLUSION CRITERIA
• To qualify for enrollment in this study, dogs must:
  • Have a diagnosis or presumed diagnosis of intervertebral disc herniation.
  • OR be neurologically and orthopedically normal (control group)
  • < 15 kg and of chondrodystrophic breeds

STUDY DESIGN
Affected Dogs
• Patients will be screened for eligibility, affected dogs with acute SCI and T3-L3 myelopathy secondary to IVDE are eligible. Dogs will receive a gait score prior to enrollment in the study. Dogs will undergo medical or surgical management of their IVDE at the discretion of their primary clinician, and may be enrolled in the study regardless of manner of treatment. It is, however, anticipated that most dogs will undergo surgical decompression via hemilaminectomy for treatment of their IVDE.

• If enrolled, dogs will be asked to perform the following list of tests at 3 time points: 3, 10 and 30 days post injury.
  • Behavioral Assessments: gait scoring, cat walk assessment, Electronic von Frey anesthesiometry. recheck physical and neurologic exam

CLIENT COMPENSATION
The sponsor will cover study associated costs for screening and recheck visits plus a $200 credit at the end of the study.

CONTACT INFORMATION
Please contact the Clinical Trials Office at the Veterinary Medical Center for more information about this study.
Please click on the links below or visit our website to find out more information about these and other clinical trials.

**Canine**

**Critical Care**
Assessment of coagulation before and after packed red blood cell transfusion in dogs using thromboelastography

**Orthopedic Surgery**
Evaluation of Novel Spinal and Orthopedic Devices in the Dog

**Radiology**
Computed Tomography for Evaluation of Canine Intestinal Obstruction

**Oncology/Radiation Oncology**
A Pilot Study of Vinblastine/Palladia Therapy for Canine Transitional Cell Carcinoma
Kit mutation and localization status as response predictors in canine mast cell tumors treated with toceranib or vinblastine: A multi-center response-adaptive randomized trial

**Dermatology/Otology**
Brainstem auditory evoked response testing in normal hearing cavalier king charles spaniel dogs

**Feline**

**Cardiology**
Acute effect of Ivabradine, a novel I-f current inhibitor, on dynamic obstruction of the left ventricular outflow tract in cats with preclinical hypertrophic cardiomyopathy

**Equine**

**Orthopedics**
Cell-Mediated Bone Morphogenetic Protein Gene Therapy for Bone Healing in Horses

**Ophthalmology**
Histological effect of semi-conductor diode laser trans-scleral cyclophotocoagulation on urophthalmic equine globes

**Upcoming Studies**

**Oncology**
Several new studies are being developed and will begin enrollment later this year

**IMED**
Association between Helicobacter pylori infection and uremic gastritis in dogs
• The purpose of this study is to investigate whether stomach changes in dogs with CKD are similar to those noted in people with CKD and Helicobacter infections, and determine if anti-Helicobacter pylori treatment improves clinical signs and prognosis in dogs with CKD.
Improving outcome in dogs with glomerular disease via pharmacodynamic-based dosing of enalapril

One in five pet dogs will develop kidney disease at some point. Proteinuric glomerular diseases may be the underlying cause of chronic renal failure in at least 50% of canine patients with chronic renal failure. Glomerular disease is a type of kidney disease in which the parts of the kidney (glomerulus) that help filter waste and fluids from the blood and keep protein from being removed is damaged. Proteinuria (protein in the urine) is the first indicator that there is a kidney problem.

This study will evaluate the effectiveness of giving a higher dosage of Enalapril to dogs suffering with kidney disease. Enalapril is an angiotensin converting enzyme inhibitor (ACE inhibitor or ACEi). What this means is that enalapril stops the angiotensin converting enzyme from producing a compound called angiotensin-II, which is a potent vasoconstrictor. Vasoconstrictors cause the narrowing of blood vessels which ultimately leads to decreased blood flow. Enalapril acts as a vasodilator because it blocks the production of angiotensin-II. Essentially, by acting as a vasodilator, enalapril acts to increase the diameter of the blood vessels instead of narrowing them. This increase in the diameter of the blood vessels results in increased blood flow. Enalapril can aid in increased blood flow to the kidneys, which has been shown to be beneficial to dogs that are experiencing kidney disease. It is believed that enalapril and other ACE inhibitors probably decrease the amount of protein that is allowed to escape through the kidneys and into the urine. The current recommended enalapril dose was established using 75% suppression of ACE activity as the desired pharmacodynamic end-point; however, recent studies in people suggest that higher ACEi doses required for maximal reduction in urine protein excretion may dramatically improve patient survival. Data collected from this study will not only benefit dogs but humans as well.

INCLUSION CRITERIA/CLIENT COMPENSATION

Dogs must have primary glomerular disease. They cannot be diagnosed with nephrotic syndrome, a concurrent disease that will alter kidney function or any condition that would result in less than 12 months of survival. Your dog’s urine protein:creatinine ratio must be greater than or equal to 3.0. All other labwork will need to be within normal range. Owners must commit to returning to OSU for regular recheck appointments. The duration of the study is roughly 36 weeks with a variation of appointments depending on which group your dog is placed into. The study sponsor will cover all cost associated with the study once your pet is enrolled, however the owner is responsible for initial screening visit, purchase of enalapril, and any other medications needed for standard treatment of their dog’s kidney disease. If any unforeseen events occur these cost are covered up to $1000.

If you have questions, concerns or would like to schedule an appointment please contact:

Dr. Barrak Pressler
(614) 292-5337
barrak.pressler@cvm.osu.edu
or
The Clinical Trials Office
(Nicole Stingle or Tamra Mathie, clinicaltrials@cvm.osu.edu)
The primary objective of this clinical trial is to evaluate the safety and tolerability of KUN C01 given to dogs with solid tumors (carcinomas, sarcomas, mast cell tumors, melanomas) and the secondary objective is to describe the antitumor response in tumor-bearing dogs.

KUN C01 is a mixture of plant extracts that includes Rhus verniciflua, Ulmus hollandica, Polygonatum facatum, Lycium barbarum, Ganoderma ucidum, and Panax ginseng. Antiproliferative activities of KUN C01 were studied in the laboratory using mouse and human cancer cell lines demonstrating inhibition of the ability of these cells to grow. KUN C01 has been tested in ddY mice administered at 2.5 and 5 g/kg once per day without any sign of toxicity. It has also been administered safely to two dogs with cancer on a compassionate use basis without any obvious side effects. The antiproliferative effects of KUN C01 are believed to be due to the components luteolin and apigenin. Luteolin has shown to induce death of cells related to inhibition of Vascular Endothelial Growth Factor production and a reduction in Aurora B kinase activity blocking proliferation of cancer cells. Apigenin induces death by inhibiting STAT3 and decreases cell viability and telomerase activity in human leukemia cell lines. In addition, it has cancer preventative effects against selected carcinogens.

**INCLUSION CRITERIA/CLIENT COMPENSATION**

To qualify for enrollment in this study, dogs must have:

- Histologic or cytologic diagnosis of cancer (biopsy or needle aspirate)
- There is at least 1 tumor (carcinoma, sarcoma, mast cell tumor, melanoma) which can be measured (minimum 1 cm in diameter)
- Generally feeling well (i.e. eating, drinking, ambulating on their own, etc.)
- No evidence of an active bacterial infection requiring antibiotics (other than topical medications) in the past 7 days
- No anti-cancer therapy within the past 21 days. This includes chemotherapy, radiation therapy, prednisone (or other forms of corticosteroids), and immunotherapy
- No tumors where abscess (infection) would result in major symptoms

All costs associated with the study are covered once the patient has been enrolled.

For more information email: Francisco.ClementeVicario@cvm.osu.edu

Phone: 614-688-5713 or 614-292-4559

The Ohio State University College of Veterinary Medicine
Spotlight Patient- Casey

Casey is an 8 year old Brittany spaniel who presented to the OSU-VMC for chronic left-sided facial pain in October of 2012. His owners noticed Casey was having trouble picking up and chewing his food and that he was painful when his face was touched. Casey had a CT performed and was diagnosed with a mass in his left nasal cavity. Casey’s owners were given all of their options for treatment and chose to enroll him into the Canine Nasal Carcinoma clinical trial. He underwent 10 treatments of radiation therapy and was started on an oral cancer therapy approved by the FDA in 2009 called Palladia (toceranib). Casey is back to his good old playful self. He has air flow back in his left nasal cavity and has enjoyed a winter of running and playing fetch in the snow. His owners are more than pleased with his recovery. In February Casey returned for his recheck CT and it showed that the mass has gotten even smaller. Casey continues to do well and is currently receiving the Palladia therapy as part of this clinical trial.