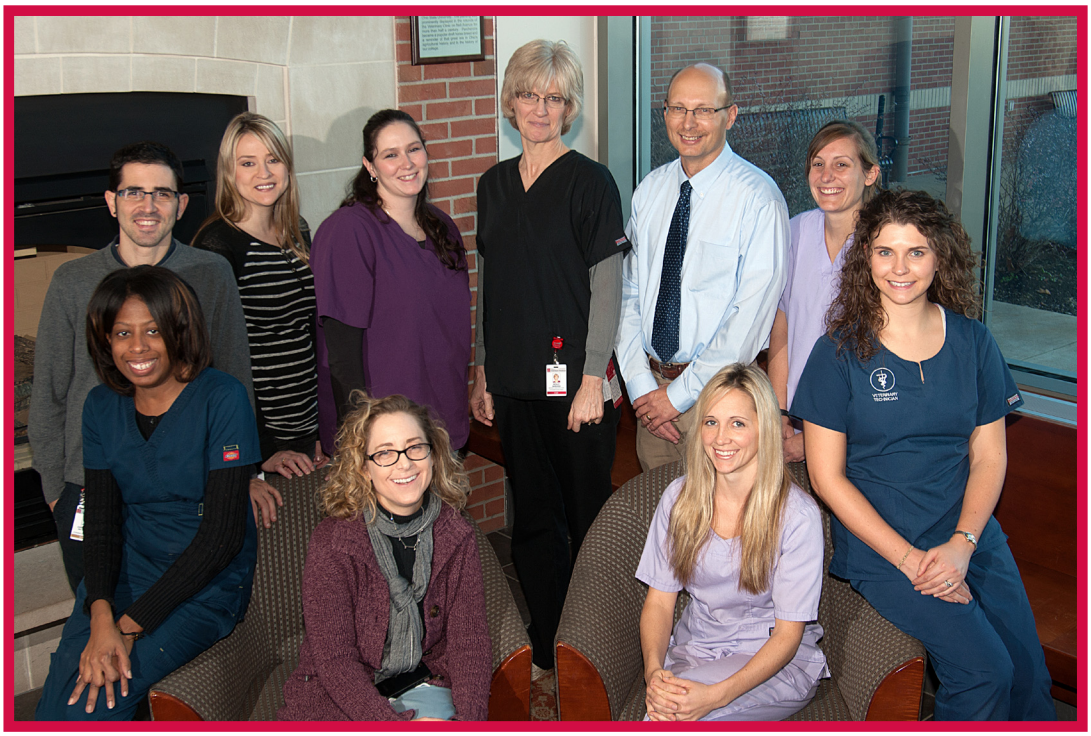
Clinical Trial Updates

Advancing the Health of Animals and Humans

November/December 2012



Clinical Trials

The Clinical Trials Office coordinates studies ranging from heart problems to eye diseases, cancer to neurological problems, all in pursuit of life-saving discoveries.

Clinical trials represent the cutting edge of medicine: research expertise meets new treatments and improved outcomes, including an improved understanding of the diseases that affect our animals and best friends

Biospecimen Repository

The Tissue Bank (Biospecimen Repository) collects samples of tumors and normal tissue from dogs and cats, and stores these tissues under controlled conditions for future use by multiple investigators. The Tissue Bank at The Ohio State University was selected by the Canine Comparative Oncology Genomics Consortium (CCOGC) as one of three veterinary institutions nationwide to participate in populating the Pfizer-CCOGC multi-institutional Tissue Bank. This National Cancer Institute-sponsored endeavor emphasizes the importance of comparative oncology research. The Tissue Bank at The Ohio State University follows the guidelines established by the CCOGC for several specific types of tumors and similar established protocols for other tumors. Tissues are collected and archived only after receiving consent from the owners. This sample bank will serve as a tremendous resource with the ultimate goal of developing new prevention and treatment strategies for dogs with a variety of illnesses.

Our Purpose

The Clinical Trials Office (CTO) provides assistance in the design, execution, and evaluation of veterinary clinical trials using client-owned animals, with the overriding goal of advancing the diagnosis and treatment of disease in veterinary patients while enhancing the health of humans.

The Ohio State University Veterinary Medical Center

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VETERINARY MEDICAL CENTER

THE OHIO STATE UNIVERSITY

An Exploratory Study of the Oral Selective Inhibitor of Nuclear Export (SINE) KPT-335 in Dogs with Lymphoma

PURPOSE OF STUDY

The purpose of this study is to evaluate the safety and antitumor activity of KPT-335 in dogs with lymphoma, either newly diagnosed or in first relapse after completion of a single chemotherapy protocol (multi-agent or single agent).

BACKGROUND

A study of KPT-335 was performed in dogs with cancer and the dose of 1.5 mg/kg was found to be well-tolerated over 4-20 weeks of dosing when given on a Monday/Wednesday/Friday (MWF) basis. In dogs with lymphoma, partial shrinkage of lymph nodes and stable disease were noted in over half of the patients treated. Side effects from KPT-335 given at this dose on a MWF basis included mild loss of appetite, occasional vomiting, and diarrhea, with some dogs experiencing an increase in thirst and an increase in urination. All of these side effect were mild and well-controlled with additional medications.

INCLUSION CRITERIA

To qualify for enrollment in this study, dogs must:

- Dogs with lymphoma, either newly diagnosed or in first relapse after completion of a single chemotherapy protocol (multi-agent or single agent). Both B and T cell accepted
- Dogs must have progress disease (measurable lymph nodes)
- Adequate organ function as indicated by standard laboratory tests
- Dogs must have an estimated life expectancy of at least 28 days.
- Prior chemotherapy or radiation must be completed at least 2 weeks prior
- Owner must be able to orally administer drug according to designated schedule
- No evidence of brain metastasis
- Cannot be less than 2 weeks from a major surgical procedure

STUDY DESIGN

- Your dog will receive KPT-335 given at a dose of 1.5 mg/kg orally once on Monday/Wednesday/Friday (MWF) of each week. Your dog will return weekly for the first 4 weeks, then every other week thereafter if your dog has experienced a complete response, partial response, or stable disease following treatment. Analysis for tumor response will be performed by direct tumor measurement or through the use of x-rays or ultrasound.

- Standard bloodwork will be performed at the beginning of each cycle. Additional tests to be performed include blood draws for measurement of KPT-335 plasma concentrations one hour after administration and fine needle aspiration of the lymph nodes to determine how CRM1 is affecting various proteins in the lymphoma cells.

- 5 dogs will stay overnight on the third week (Day 14) so that blood samples can be drawn over 24 hours to assess how KPT-335 blood levels change during the course of the day, to determine how KPT-335 affects blood levels of proteins associated with inflammation, and to evaluate CRM1 expression in blood cells. You will receive a credit of $500 for the treatment of your dog at the Veterinary Medical Center for participation in the overnight study.

CLIENT COMPENSATION

The sponsor will cover study associated costs for screening, exam fees, labwork and adverse events.

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 intially 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 Clincal Trials Office at 614-688-5713 or 614-247-8706
clinicaltrials@cvm.osu.edu

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

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.

We expect our results to provide multiple valuable outcome measures by which to document sensory and motor improvement in dogs with SCI. Based on preliminary data, we expect sensory testing to delineate insensate zones from normal thresholds, Catwalk data will show increasing dyscoordination with increasing SCI severity, and BBB scores will correlate with locomotor scores from a previously validated scale. This study may provide rapid clinical benefit to dogs with SCI by allowing veterinary researchers to "speak the same language" as bench-top researchers and federal agencies regarding treatment effects in therapeutic trials, opening the door to federal funding to study canine SCI by validating outcome measures necessary to draft competitive research proposals.

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

Normal Dogs

- Patients will be screened for eligibility, if enrolled, dogs will be asked to perform the following list of tests during each testing session with a 1 hour resting period between testing. Normal dogs will undergo each behavioral test three times, on three separate occasions, at least 24 hours apart.
- Behavioral Assements: Gait scoring, cat walk assessment, Electronic von Frey anesthesiometery

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 Assements: gait scoring, cat walk assessment, Electronic von Frey anesthesiometery
- 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

Orthopedic Surgery

Evaluation of Novel Spinal and Orthopedic Devices in the Dog

A Randomized Clinical Trial of Cemented versus Cementless Total Knee Replacement (TKR) in Dogs

Radiology

Computed Tomography for Evaluation of Canine Intestinal Obstruction

Oncology/Radiation Oncology

Examining the Efficacy of Toceranib Phosphate (Palladia) as a Primary and/or Adjuvant Agent in the Treatment of Canine Nasal Carcinoma

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

Evaluation of KUN C01 in dogs with spontaneous solid tumors

Evaluation of four STA-1474 dosing regimens in dogs with mast cell tumors

Neurology

The role of hsp70, IL-1ß and TNF- α responses in recovery after canine spinal cord injury; a pilot investigation

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

Oncology

Palladia or Palladia plus Radiation Therapy in Cats with Oral Squamous Cell Carcinoma

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 buphthalmic equine globes

Upcoming Studies

Oncology
Several new studies are being developed and will begin enrollment in the new year.

Dermatology
Efficacy of a Vaccine against a key cytokine involved in canine atopic dermatitis as an Aid in Reduction or Control of Clinical Signs Associated With Canine Atopic Dermatitis

- Study covers the costs associated with the study at each visit
- Advantage Multi for Dogs will be supplied during the study

Please contact Dr. Hillier about potential patients at hillier.4@osu.edu or 614-292-3551

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.

Efficacy of a Vaccine against a key cytokine involved in canine atopic dermatitis as an Aid in Reduction or Control of Clinical Signs Associated With Canine Atopic Dermatitis

The purpose of this study is to evaluate whether this vaccine reduces the clinical signs and pruritus associated with canine atopic dermatitis.

BACKGROUND:

The targeted cytokine has been implicated in the pathogenesis of atopic dermatitis in humans. It has been shown that vaccination of beagles and mongrels against the targeted cytokine elicits an antibody response detectable by enzyme-linked immunosorbent assay (ELISA). More importantly, the elicited antibodies block the in vitroactivity of the targeted cytokine.

STUDY DESIGN:

The objective of this study is to evaluate the effect of a key cytokine involved in canne atopic dermatitis on the severity of clinical signs associated with atopic dermatitis in client-owned dogs. For this purpose, a group of 20 dogs will be vaccinated 4 times, at a 21 day-interval, with the vaccine(250 µg/dose)adjuvanted with 15% Emulsigen. A second group of 20 dogs will be vaccinated 4 times with a placebo containing the same adjuvant. The vaccine and placebo will be administered as a 1-mL dose by subcutaneous route. Sera will be collected from all animals at regular intervals. The antibody response against the cytokine will be evaluated in collected sera using antigen-specific ELISA. Sera will also be tested for their capacity to block the activityof the cytokinein an in vitro cell proliferation assay. The primary measures of vaccine efficacy will be based on statistical evaluation of 1) reduction of atopic dermatitis skin lesion scores, as measured by a decrease from baseline of Veterinarian's assessed lesions and 2) reduction of pruritus, as measured by a decrease from baseline of owner's assessed scores.

INCLUSION CRITERIA:

The study will enroll client-owned dogs with a history of nonseasonal or seasonally non-seasonal Atopic Dermatitis. To be included in the trial, dogs must fulfill the following criteria:
1. Owner's written informed consent has been obtained.
2. At least 18 months of age at start of trial.
3. History of non-seasonal or seasonally non-seasonal pruritus.
4. Clinical diagnosis of atopic dermatitis.
5. Incomplete response to a minimum 6-week hydrolyzed diet or novel protein exclusion diet (home cooked or commercial). Dogs should be stabilized on a diet for at least two weeks prior to enrollment in the study and this diet should be maintained throughout the trial.
6. Incomplete response to a regulatory approved flea control regimen for at least 8 weeks. Regardless of whether there is an element of flea allergy dermatitis (FAD), monthly flea control must be maintained throughout the trial.
7. Dogs must be on a regulatory approved endoparasite control program, including heartworm for at least 8 weeks and must continue this program throughout the trial.(All study particiapants will have Advantage Multi)
8. Sarcoptic mange excluded by trial therapy, negative serology, or history and clinical signs.
9. Within 30 days prior to study initiation, demonstrate immediate positive skin reactions upon intradermal testing with environmental allergens such as house dust mites, pollens, or molds or exhibit high serum concentration of allergen-specific IgE.

Efficacy of a Vaccine against a key cytokine involved in canine atopic dermatitis as an Aid in Reduction or Control of Clinical Signs Associated With Canine Atopic Dermatitis- Cont'd

10. No clinical signs suggestive of overt surface, superficial, or deep microbial skin infection (i.e. bacterial pyoderma and Malassezia dermatitis) at the time of entry. Dogs with bacterial or fungal skin infection are eligible for inclusion in the study only after resolution of their infections.
11. Dogs must exhibit cytokine or cytokine receptor mRNA in biopsies obtained from their lesional skin.
12. Baseline Pruritus Visual Analog Score (PVAS) of > 4.
13. Allergen-specific immunotherapy is permitted if used for >12 months, the dose remains unchanged for 6 months, the clinical signs are stable and the regimen is maintained during the trial.
14. Essential fatty acid supplementation to diets is permitted if in use for > 8 weeks, the clinical signs are stable and the dosing regimen is maintained during the trial.

EXCLUSION CRITERIA:

Dogs with the following criteria or conditions will be excluded from the study:
1. Pregnancy, lactation or breeding activity.
2. Evidence of underlying disease that may compromise the study outcome.
3. Disease history and results of diagnostic testing are not clearly documented.
4. Dogs not using a regulatory approved flea control and endoparasite (including heartworm) control regimens.
5. Diet changes during the trial.
6. Use of anti-inflammatory drugs other than those allowed by protocol.
7. Allergen-specific immunotherapy discontinued within 6 months or initiated within 12 months prior to enrollment.
8. Initiated or discontinued essential fatty acid supplementation within 8 weeks.
9. Clinical evidence of active ectoparasite infestation.
10. Clinical evidence of active bacterial or fungal skin infections.

CLIENT COMPENSATION:

- Study covers the costs associated with the study at each visit
- Advantage Multi for Dogs will be supplied during the study

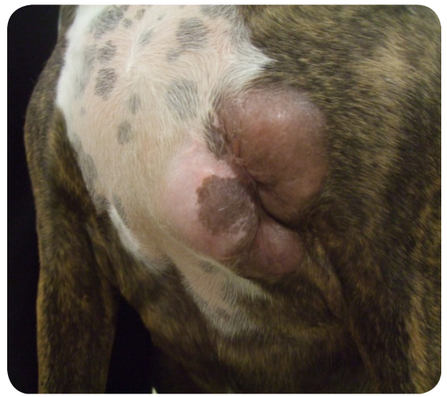
CLIENT COST:

- Clients that complete the study will have a credit of $300 to be used at the OSU Veterinary Medical Center

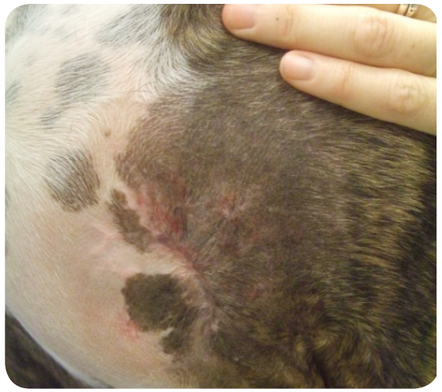
Contact: Dr. Hillier (hillier.4@osu.edu) or Nicole Stingle (ClinicalTrials@cvm.osu.edu)

Spotlight Patient- Winston

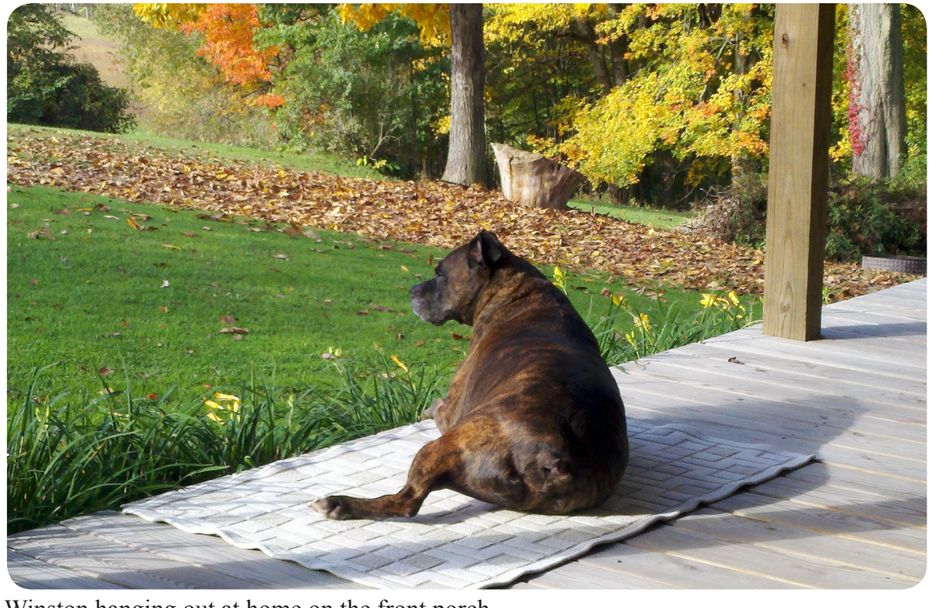
Winston is an 8-year-old mixed breed dog who presented to the OSU-VMC Medical Oncology Service for evaluation of a mast cell tumor that was present on the left side of his chest. The tumor had been removed twice and had grown back both times, and now was quite large. Winston was entered into the STA-1474 clinical trial evaluating a new heat shock protein 90 (HSP90) inhibitor in dogs with mast cell tumors. He did very well throughout the 5 week study, and his tumor was almost completely gone by the end of his treatment. Winston has just finished a course of radiation therapy to hopefully get rid of any remaining tumor cells and is now enjoying his time hanging out on the front porch. Thanks to Winston and his family for helping us with this study!



Before STA-1474



After STA-1474



Winston hanging out at home on the front porch.

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:creatnine 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 unforseen 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)

Please Welcome Our New Staff!

Annie Adrian

The CTO would like to welcome Anna (Annie) Adrian to our office as the new Administrative Program Assistant. Annie is from London Ohio. She has some animal background with horses being her main focus. Horses are both her hobby and life. She loves doing everything with them. She is married and has a daughter. They reside out in the country close to Mt. Sterling. She says "I think I am a well-rounded person with some knowledge in several areas pertaining to the job."

We are happy to have Annie join our team!

Happy Holidays

From,
Everyone at the Clinical Trials Office

The Clinical Trials Office is Expanding!!

The Clinical Trials Office has received funding to start construction and renovations to expand a new staff office to 1000 sq. ft., in addition to expanding the tissue bank. The office has recently partnered with the Comprehensive Cancer Center and was awarded a Program Project Grant working with Nationwide Children's Hospital.

Newsletter designed by Nadia Ruffin ruffin.15@osu.edu