Improving outcome in dogs with glomerular disease via pharmacodynamic-based dosing of enalapril

The Clinical Trials Office at The Ohio State University Veterinary Medical Center is currently enrolling dogs for a clinical trial evaluating the effective dosage of enalapril in treating glomerular disease in dogs.

Recent data suggests that one in five pet dogs will develop kidney disease at some point in their life, and proteinuric glomerular diseases may be the underlying cause of chronic renal failure in at least 50 percent of canine patients with chronic renal failure. Suppression of the renin-angiotensin-aldosterone system via administration of angiotensin converting enzyme inhibitors (ACEi) reduces urinary loss of proteins, and is the mainstay of glomerular disease treatment in both dogs and people. Lower urine protein concentrations are associated with slower declines in glomerular filtration rate (GFR) and longer survival times. Enalapril has been successful in decreasing urine protein excretion and has been used to treat glomerular disease in both humans and dogs. However, recent studies in humans suggest that higher ACEi doses can significantly improve patient survival.

The goal of this study is to determine whether the dosage of enalapril in treating glomerular disease in dogs.

It is anticipated that dogs treated with enalapril at doses which maximally reduce urine protein excretion will live longer and have a slower rate of GFR decline than those receiving the standard drug dose. In order to be eligible for this study, dogs must have primary glomerular disease and a UPC less than or equal to 3.0; dogs cannot have a serum creatinine concentration greater than 1.5 mg/dl or nephrotic syndrome, be diagnosed with any concurrent disease that alters kidney function, or have any concurrent disease that will likely result in less than a year of survival.

Given that the cumulative lifetime incidence of kidney disease is almost 20 percent, thousands of animals per year may potentially benefit from this study. Longer-term benefits include the ability to compare enalapril to newer non-ACEi anti-proteinuric therapies.

This study is being led by Dr. Barrak Pressler, assistant professor of Small Animal Internal Medicine in the Department of Veterinary Clinical Sciences. Dr. Pressler earned his DVM in 1999 from the University of California, Davis and following a residency in Small Animal Internal Medicine at North Carolina State University was a Post-Doctoral Fellow in the Division of Nephrology and Hypertension at the University of North Carolina, Chapel Hill School of Medicine from 2004-2006.

go.osu.edu/enalapril

Cats needed for cardiology studies

Feline patients with hypertrophic cardiomyopathy (HCM) are being sought for two different clinical trials, led by veterinary cardiologist Dr. Karsten Schober, associate professor of Veterinary Clinical Sciences.

One study focuses on the acute effect of a novel cardiac inhibitor, ivabradine, on dynamic obstruction of the left ventricular outflow tract in cats with preclinical HCM. Currently, atenolol and diltiazem are used to treat preclinical HCM. However, both drugs may cause weakness, fainting, loss of appetite, cough, and weight loss.

Ivabradine is a novel agent that is clinically well tolerated in cats, and might become a new treatment option in cats with HCM.

The second study evaluates the effects of pimobendan in cats with HCM and congestive heart failure (CHF), with and without left ventricular outflow tract obstruction. This study will assist in gathering data on drug tolerability, the effect of clinical signs and survival, and other parameters to plan future studies.

go.osu.edu/catCHFstudy

vet.osu.edu/vmc
Compassionate use of KPT-276 in dogs with spontaneous tumors

This study will focus on dogs diagnosed with lymphoma, mast cell tumor, metastatic osteosarcoma, or melanoma. The patient may have failed standard therapy or there may be no other known effective antineoplastic therapeutic options, or the owner may elect to enter the patient in lieu of standard therapy. Additionally, the dog must be at least one year of age; have adequate organ function as indicated by standard laboratory tests; have an estimated life expectancy of at least 28 days; have no evidence of brain metastasis; prior chemotherapy or radiation must be completed at least two weeks previously; and the owner must be able to orally administer the drug according to the designated schedule.

The dogs enrolled will be administered KPT-276 orally three days per week for four weeks. Depending on tolerability, the regimen may be altered. The drug will be administered on an empty stomach by the owner at home at the same time each morning. Patients will need to return every seven days for two to four weeks. On these days, the patient will need to arrive within two hours of administering medication for blood work.

Dr. Cheryl London, associate professor of Veterinary Biosciences and the Thekla R. and Donald B. Shackelford Professorship in Canine Medicine, is an accomplished comparative veterinary oncologist. She has been involved in numerous cancer studies and has significantly improved upon what is known about neoplasias. Currently, Dr. London is enrolling dogs for a clinical trial testing the effective dose of KPT-276. KPT-276 is an anti-cancer drug that prevents the ability of neoplastic cells from eliminating anti-cancer drugs from the cell.

Fine-tuning the treatment for equine glaucoma

Glaucoma is a common vision-threatening sequela to Equine Recurrent Uveitis. The glaucomas are a group of diseases resulting from alterations in the drainage of aqueous humor, which causes an increase in intraocular pressure (IOP) that interferes with normal function of the retina and optic nerve. This often results in retinal and optic nerve degeneration, blindness, and variable degrees of pain. Previous studies have proven that the diode laser trans-scleral cyclophotocoagulation (TSCP) has the capability of providing long-term IOP reduction for equine glaucoma. Currently, the energy and time settings as well as the anatomic position for the diode laser TSCP are based on studies previously done in normal horse eyes. However, this may not relate well to the proper position in the glaucomatous eye because as the eye increases in size with chronic glaucoma, the ciliary body (the tissue that is targeted by laser surgery) may move in position. Therefore, the goal of this study is to determine if the currently used location and energy setting for the diode laser TSCP are correct for treatment of equine glaucoma.

Dr. Anne Gemeinsky Metzler, professor of Comparative Ophthalmology in the Department of Veterinary Clinical Sciences, is enrolling horses for this study that have a blind glaucomatous eye and whose owners have already decided to undergo general anesthesia to have the eye removed. Axial globe length and corneal dimensions will be measured and routine TSCP will be performed immediately prior to enucleation. Histopathology will then be performed on the eye to evaluate the laser effects on the globe.

goa.edu/equine-uveitis

Modern lameness evaluation and treatment at the Galbreath Equine Center

Equine force plates are being used more frequently for research studies, and also in clinical practice as a means of diagnosing mild lameness and differentiating between neurologic deficits or musculoskeletal problems. The force plate has been applied for equine lameness evaluation as it can provide more sensitive, objective, and quantitative gait assessment, compared to subjective lameness grading scales. Dr. Alicia Bertone and Dr. Akikazu Ishihara have worked together on numerous clinical trials using the equine force plate at the Galbreath Equine Center at The Ohio State University Veterinary Medical Center.

Currently, they are recruiting horses with a confirmed diagnosis of osteoarthritis for a study on the use of autologous blood solution for treatment of equine osteoarthritis. This study will use the force plate as a means of objective qualification of lameness before and after treatment.

Platelet and blood therapy is an emerging new technology being used as a biologic therapy. Studies show that the growth factors in platelets, plasma and white blood cells can facilitate tissue repair.

goa.edu/equine-osteoarthritis

Platelets from blood, while well known to be responsible for clotting, also contain a variety of growth factors that have been shown to promote wound healing. Some studies in humans have shown that platelet therapy may benefit patients with osteoarthritis, but studies in horses and dogs are lacking. This study will test the ability of a concentrated, activated, autologous blood solution to increase therapeutic mediators in joints and reduce lameness in horses with osteoarthritis.

Published studies completed at Ohio State using the equine force plate for lameness evaluations include “Use of kinetic gait analysis for detection, quantification, and differentiation of hind limb lameness and spinal ataxia in horses”,” Anti-inflammatory and analgesic effects on intra-articular injection of triamcinolone acetonide, mepivacaine hydrochloride, or both on lipopolysaccharide-induced lameness in horses”, and “Association between subjective lameness grade and kinetic gait parameters in horses with experimentally induced forelimb lameness.”

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considered are 12, 24, 36, and 52-week survival rates, rate of GFR decline, and onset of azotemia in dogs receiving higher dosages of enalapril as compared to the standard enalapril dose.

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I have now completed seven months as the director of the Veterinary Medical Center and I am still amazed by the breadth and depth of the work that goes on here. I appreciate this opportunity to reach out to you- our partners in patient care, our referring veterinarians that help make our work possible.

In this issue of Update for Veterinarians we are featuring our Clinical Trials Office and highlighting many of the studies that are advancing care for companion animals and horses. You can always view an updated list of studies at go.osu.edu/clinical-trials.

There are many benefits to referring your clients and patients to an academic veterinary medical center. The clinical trials here at Ohio State allow us to help your clients through constant innovation and state-of-the-art care. By offering clinical trials, we are able to stay at the forefront of veterinary medical knowledge and to offer novel therapies unavailable anywhere else.

Studies currently underway at the Veterinary Medical Center range from treating congestive heart failure to understanding equine eye diseases; from studying better pharmaceutical treatments for cancer to unlocking the secrets of neurological problems. We can work together to find new or alternative treatments for your client’s beloved animals. Thank you for partnering with us to ensure that advancements in veterinary medicine continue while providing state-of-the-art care for out patients.

From the Director

Cats needed for cardiology studies

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