Clinical Trials

New Clinical Trials

The Oncology Service has opened two new clinical studies this spring. They are:

- Evaluation of the mTOR Inhibitor Rapamycin in Dogs with Osteosarcoma
- Mapping Genes Associated with Canine Mast Cell Tumors (MCT).

Both clinical studies are being conducted in conjunction with other institutions. Descriptions of each study are included in this newsletter and are on our website.

Ongoing Clinical Trials

- Gene expression profiling of canine lymphoma
- Oral artemisinin in dogs with spontaneous tumors
- Copy number polymorphisms in dogs
- DNA methylation in canine lymphoma
- Rapid release paclitaxel particles for intravesical treatment of transitional cell carcinoma

More information on all the clinical trials can be found at the following website: www.vet.osu.edu/565.htm or by contacting the Oncology Service at (614) 292-3551.

Mapping Genes Associated with Canine Mast Cell Tumors

This study is being conducted at the Ohio State University College of Veterinary Medicine in conjunction with the Massachusetts Institute of Technology. The goal of this study is to map genes associated with Mast Cell Tumors (MCT) by obtaining genomic DNA from blood collected from Labrador Retrievers and Golden Retrievers. We will be collecting blood from dogs diagnosed with MCT disease and from healthy breed-, sex-, and age-matched controls. In the future, blood from other breeds known to develop milder forms of the disease may also be collected for evaluation.

Historically, considerable work has been done to provide better prognostic indicators for the biological behavior of canine MCT, such as tumor grade, proliferation indices, tumor location and clinical history. However, there is still no clear prognostic indicator to identify a biologically aggressive MCT.

Certain breeds, such as Golden Retrievers, have an increased incidence of MCT. This breed-associated increased incidence rate suggests a genetic component to the disease. We will use a new approach to identify genes associated with increased risk for MCT. Once the genes are identified, it is hoped that genetic tests for carriers of MCT predisposition and identification of disease gene mutations can be developed.
Evaluation of the mTOR Inhibitor Rapamycin in Dogs with Osteosarcoma

This trial is a multi-center national trial sponsored by the National Cancer Institute (NCI), Comparative Oncology Program, Comparative Oncology Trials Consortium, and the Morris Animal Foundation. The purpose of this study is to define a relevant dose and dosing schedule for Rapamycin in tumor bearing dogs. This is a dose escalation study (7 days) of Rapamycin in dogs with osteosarcoma (OSA) prior to resection/amputation. Serial pre- and post-treatment tumor biopsies will allow for assessment of tumor biomarkers, which will be correlated with serum biomarkers. After completion of this first phase, future studies will assess the anticancer activity of Rapamycin in dogs with metastatic OSA, alone and in combination with conventional chemotherapy.

Rapamycin has been shown to inhibit mTOR activity, a pathway believed to be important for cancer progression and resistance to therapy. The NCI has shown that mTOR inhibition in human sarcoma cell lines has resulted in suppressed cancer cell proliferations and suppression of the metastatic cell types. Rapamycin currently is approved as an immunosuppressive agent for patients undergoing organ and bone marrow transplants. Its use in dogs has been limited due to their sensitivity to the drug; at higher doses it may cause gastrointestinal problems (potential adverse effects are listed below). However, therapeutic levels of Rapamycin have been safely achieved in dogs following low-dose administration of the drug.

The study timeline will include the following:
1) An initial appointment to assess study eligibility, baseline imaging, possible cytology and blood work
2) After enrollment, a pretreatment biopsy and serial whole blood samples (6 ml each) will be obtained at each of the following time points: 30 minutes, 1, 2, 6, 24, and 48 hours after the initial dose of Rapamycin. This visit will include an overnight stay at The Ohio State University Veterinary Teaching Hospital (OSU-VTH) for monitoring, with a return visit the next day
3) Subsequent doses will be given in one of the following ways:
   - At home by the owner for 7 days, as an intramuscular injection.
   - Return to (OSU-VTH) for daily injections
   - Your dog will board at the hospital for one week and the injections will be given by the oncology staff.
4) Return to (OSU-VTH) for surgery on Day 8 for primary tumor resection/amputation. Blood collection will be done 24 and 48 hours after last dose
5) Return to (OSU-VTH) on Day 15 (1 week post surgery) for evaluation and blood collection

After the Day 15 visit, your dog can receive any adjuvant chemotherapy protocol. Your clinician will discuss the appropriate chemotherapy protocol for your dog. All visits after the initial visit to establish eligibility will be covered by the study with the exception of surgery. The study will cover $1000 towards the cost surgery but the remainder of the surgical cost would need to be covered by owners. The study does not cover any adjuvant chemotherapy following surgery.

Molecular structure of Rapamycin
Meet Oncology team member Francisco Alvarez, DVM, MS

Dr. Alvarez completed a residency in Small Animal Oncology at The Ohio State University in 2006. He graduated with honors from the National University of Mexico where he received his Doctor of Veterinary Medicine and Master's of Science degrees. In 2006, Dr. Alvarez successfully defended his Masters thesis, entitled 3-Phosphoinositide-Dependent Protein Kinase-1 (PDK-1)/Akt Signaling and Inhibition in a Canine Prostate Carcinoma Cell Line in the Department of Veterinary Clinical Sciences at OSU. Dr. Alvarez received the College Veterinary Medicine, Teaching Hospital Service Award in 2006.

Dr. Alvarez has joined the Small Animal Oncology and Hematology Service as a clinical instructor. In addition to Dr. Alvarez, the service is staffed by three other oncology faculty members: Drs. Guillermo Couto, William Kisseberth and Cheryl London, three residents enrolled in an ACVIM oncology residency training program, and three registered veterinary technicians. The addition of Dr. Alvarez to the Oncology staff has allowed for the expansion of appointments, which has enabled the service to better serve veterinary cancer patients.

In addition to his work in the Oncology Service, Dr. Alvarez works closely with the Greyhound Health and Wellness Program at The Ohio State University Veterinary Teaching Hospital. He helps advise and oversees the members of the program with their Greyhound patients and Greyhound consults. He also continues his research with special interests in the following areas: osteosarcoma, lymphoma, and experimental therapeutics.

Above: Faculty composite photograph of Dr. Alvarez
Below Right: Drs. Alvarez and Fischetti administering intra-lesional chemotherapy via ultrasound guided needle to a dairy cow.
Below Left: Dr. Alvarez examining a Greyhound patient during one of the Greyhound clinic days at The Ohio State University Teaching Hospital.
**Signalment:**
A female, 10-year-old Golden Retriever presented for evaluation of a raised, pink mass on her side. The mass has been present for about 6 months. According to the owner the mass at times appears to get bigger when her dog scratches at the mass. The mass was aspirated.

**Above, Left, and Below Right:** Representative cytologies from fine needle aspirates (FNA) of tumors. Wright's-Giemsa, 100X

**Bottom left:** Photograph of the mass.

**What is your cytologic description?**

**What is your diagnosis?**

**What are your treatment options?**

The answers are on the next page.
**Review of Canine Mast Cell Tumors**

Mast Cell tumors are common malignant tumors of the skin and subcutaneous tissues in dogs. The biologic behavior of these tumors is highly dependent on the histological tumor grade. The majority of Grade 1 and some Grade 2 MCTs can be treated with wide surgical excision; however, a proportion of the Grade 2 MCTs will metastasize. Grade 3 tumors generally have a high metastatic rate. These MCTs require more aggressive treatment.

There are several other characteristics that can be used to help determine prognosis in addition to the histological grade. Some of these are tumor characteristics such as location and length of time since presentation, proliferation indices, and presence of clinical signs.

Staging for MCTs should at least include a fine needle aspirate of the mass and regional lymph nodes, even if they are not palpably enlarged. Most grade 2 and 3 MCTs should be staged further with an abdominal ultrasound which may include aspirates of the spleen and liver.

Current therapy options for MCTs, include surgical excision, chemotherapy, and radiation therapy. Radiation therapy has been shown to be effective at eliminating microscopic disease following incomplete excisions of Grade 1 and Grade 2 MCTs. Some Grade 2 and all Grade 3 MCTs require chemotherapy, such as vinblastine, CCNU (lomustine), and prednisone to treat metastatic disease with the hope of achieving better survival rates.

For information on the Clinical Trials please contact, Oncology Service (614) 292-3551 or for information concerning the Greyhound Program please contact, Liliana Marin, DVM (marin.25@osu.edu) at (614) 292-0950.

Appointments for Medical Oncology are scheduled by calling OSU-VTH at (614) 292-3551, please follow the phone prompts to reach oncology and then ask for any of the following individuals: Stacey Gallant, RVT; Nicole Westendorf, RVT; Janet Charske, RVT

Appointments for Radiation Oncology are scheduled by calling OSU-VTH at (614) 292-3551. Please ask for Eric Green, DVM, DACR (Radiology and Radiation Oncology).

**WEBSITES:**

Oncology/Hematology: vet.osu.edu/564.htm; Blood bank: vet.osu.edu/bloodbank.htm
Chemotherapy Protocols: vet.osu.edu/1359.htm; Greyhound Information: vet.osu.edu/1872.htm

You can be part of improving animals' lives through your generous donation. For information about giving to these and other programs please contact Karen Longbrake, Director of Development at (614) 688-8433 or Longbrake.1@osu.edu.